Upcycling of Medical Cannabis production and processing residues

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Upcycling of Medical Cannabis production and processing residues

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Background

Since 1 July 2018, it has been possible to apply for a license to cultivate medicinal cannabis in Denmark. The rules appear from the executive order on the cultivation, production and distribution of cannabis bulk and production of cannabis primary products. This means that companies in Denmark can now apply for a license to produce medicinal cannabis for the pilot programme and patients in Denmark and export. Currently, 40+ companies were granted permission to cultivate and handle cannabis in Denmark.

Cannabis substance and one of its derivatives were classified as Schedule IV (i.e. a subset of Schedule I drugs) which was designated in a category alongside heroin and other opioids.[1] That means not only cannabis substances were considered to be "highly addictive and highly liable for abuse," they're also labelled as "particularly harmful and of extremely limited medical or therapeutic value." Nevertheless, the UN Commission on Narcotic Drugs approved a recommendation from the World Health Organization on 2nd of December 2020 to remove cannabis and cannabis resin from its Schedule IV classification - a move that recognizes the plant as having medicinal value.[2]

The active substances (i.e. cannabinoids) in cannabis are found mainly in the trichomes which are concentrated in the flowers or buds, where these can be marketed directly or processed further for purified cannabinoids i.e. THC and CBD. The delta-9-tetrahydrocannabinol (Δ9-THC), a.k.a. to cannabis users simply as THC, is the cannabis plant's primary component for causing psychoactive effects. In 1964, Raphael Mechoulam a Bulgarian-born chemist first isolated THC and found that the substance is absorbed into the bloodstream and bound to the naturally-occurring endocannabinoid receptors located in the parts of the brain (i.e. cerebral cortex, cerebellum, and basal ganglia) responsible for thinking, memory, pleasure, coordination and movement.[3] Cannabidiol (CBD) is one of 113 identified cannabinoids (so far) in cannabis plants does not have the same psychoactivity as THC. As of 2019, clinical research on CBD included studies related to anxiety, cognition, movement disorders, and pain, but there is insufficient high-quality evidence that cannabidiol is effective for these conditions.[4]

The THC or CBD containing cannabis oils are utilized for the treatment of cancer and nausea and can also be used to improve sleep and to alleviate stress and anxiety. The legality of cannabis oils compared to buds differs from country to country. The demand for cannabis oil is rising due to social stigma involving the smoking of cannabis (marijuana). Moreover, doctors are not comfortable with patients smoking cannabis as it has potential detrimental components such as particles, tar, and other chemicals. The revenue forecast for medical and recreational cannabis is projected to increase to more than $73 billion by 2027.[5]

As the wave of legalization progresses, a cannabis production (i.e. budding), processing and extraction industry is now seeking to implement high-level of standard practices (i.e. GMP, GACP) to meet regulatory requirements for medical and pharmaceutical products. Implementing the methods and disciplines of plant science and analytical chemistry will ensure that cannabis producers can produce safe, reliable, consistent, and high-quality

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[1] Single Convention on Narcotic Drugs, United Nations 1916

[2] UN removes cannabis from a list of the most dangerous substances

[3] Gaoni Y., Mechoulam R. (1964) Isolation, structure, and partial synthesis of an active constituent of hashish. J. Am. Chem. Soc. 86:1646.

[4] Black N, et al. (2019) Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. The Lancet. Psychiatry. 6 (12): 995–1010.

[5] Medical marijuana market shares 2020 -2027

products for a rapidly growing and profitable market. On the other hand, the production and processing of cannabis also generate side stream residues that could end up as waste materials. The consequences of improper disposal can be serious for cannabis businesses, i.e. they can lose their license if verified that waste was improperly handled. Commercial cannabis has five core business models: cultivation, manufacturing, or processing (i.e. extraction), distribution, retail, and laboratory testing. Each business model has different residue (i.e. waste) streams and therefore must be dealt according to the type of business models and production activities.

Danish Cannabis producers i.e. cultivators or processors for cannabis flowers or buds, as well as THC, CBG and CBD-oil manufacturers, are facing an enormous challenge on their cannabis residues. The residues from cannabis plant cultivation are generated from routine pruning, trimming, harvest, cloning, propagation, i.e. flower, leaves, stalk or stem, root ball, failed plant, mature clone. In addition, manufacturing of THC and CBD containing cannabis oil also accumulates waste notably from the post-extraction of cannabis biomass that includes buds, flowers, leaves, trims, and shake with allowable levels of residual contaminants or with solvent residuals.

To our knowledge (from 1st Medical Cannabis Symposium, DTI Taastrup), none of the Danish Cannabis producers employs upcycling technology to valorized cannabis production and processing residues. The current management guidelines for cannabis residue in Denmark indicated that the waste generated from cannabis-related activities i.e. cultivation and manufacturing must be burned for destruction. However, like any other terrestrial plant residues e.g. agri-residue, the cannabis cultivation and manufacturing residues can be upcycled to produce high-value compounds. For instance, in the ProEnrich project has developed flexible biorefinery approach that able to process a wide range of agri-residues from rapeseed meal, olives, tomatoes and citrus fruit industries. Moreover, in the Subleem 2.0 project has established a food-grade pilot-scale biorefining plant for green biomass processing such as grasses and sugar beet leaves (e.g. tops), through which it is possible to assess the potential of refining strategies and products.

This report will deliver different upcycling technology related to plant residues that can be applied in the cannabis industry. We will outline various chemical compounds from cannabis residues that have valuable applications as well as discussed, the types of technology necessary to isolate them. The report will highlight current regulatory standards for handling cannabis waste in comparison to existing pharmaceutical manufacturing practices related to waste management. Different products and applications for Medical Cannabis will be highlighted in the report as well the various processing strategy will be reported.

The knowledge being established by this report is highly relevant not only to the Danish Cannabis Industry but also to the whole cannabis business sector. This report will provide an understanding of the different strategies for value creation to cannabis waste-stream and subsequently uphold the regulatory standards and manufacturing practices. Thus, many stakeholders will benefit from this report notably the Invest in Denmark for the cannabis business sector as well as the Danish Medical Agency for regulatory standard. Since Denmark is one of the pioneers of medical cannabis in EU, this report could serve as a knowledge resource for many businesses in the EU, Canada and the US who wants to valorize their cannabis waste.

Introduction

Current products that are generally utilized are derived from petrochemical-based building blocks. Europe imports almost 95% of its crude oil making it particularly sensitive to economic fluctuations and resource availability, not to mention negative environmental impacts of using non-renewable materials.[6] To tackle this situation, the Research and Innovation Roadmap 2050 and Strategic Innovation & Research Agenda (SIRA) have both been designed to promote a coordinated push towards sustainability of Europe's raw materials.[7, 8] Upcycling of medical cannabis cultivation and manufacturing residues correspond very well with sustainable utilization of raw and is in line with UN's Sustainable Development Goals.

Over 5000 years ago, *Cannabis sativa* L. was cultivated in Central and North-eastern Asia.[9] Today cannabis i.e. industrial hemp has been widely cultivated and used throughout history for its fibre, as well as for its nutritional and medicinal properties.[10] Hemp is an annual high-yielding crop with a low environmental impact due to its resilience to pests and diseases, making it a suitable crop for both conventional and organic cropping systems. In comparison with other crops, hemp requires a low level of irrigation and fertilizers after its establishment. The stems provide fibers and hurds or shives, while seeds are used for food, feed, and pharmaceutical applications.[11]

Understanding the different chemical components of the various parts of the cannabis plant is a prerequisite for developing upcycling strategy. The cannabis stem is a source of fibre and woody core (i.e. hurd or shives) that is high in cellulose and hemicellulose content. The underutilized seed and pressed seed meal of cannabis contain protein and polysaccharide that can be catalyzed into functional molecules. Therefore, developing cannabis biomass residues into a sustainable source of value-added biochemicals and biofuels will require a flexible cascading biorefining technology. Current biorefining technology for the extraction of cannabinoids utilized hydrocarbon solvent, supercritical fluid-CO_2, and ethanolic extraction. The downstream processes for the purification of cannabis extract concentrates may involve winterization, vacuum filtration, rotary evaporation, and short path distillation technology.

Upcycling strategy for cannabis residue may involve different conversion routes notably chemical, thermo-physical and biochemical conversion for breaking down the cell wall matrix of the plant material residues. Thus, liberating more fermentable sugars that can be utilized for fermentation of various biochemical as agent for bioenergy and bioplastic production. Although the hemp seed boasts high nutritional and functional potential, its application in food preparations is still underestimated due to scarce upcycling technology and the presence of several anti-nutritional factors. However, the employment of bioprocessing technology enhances the antioxidant activity of the hemp in vitro. The lactic acid bacteria fermentation was the best method to significantly improve the antioxidant

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6 Eurostat (2020) Oil and petroleum products - a statistical overview. Data extracted June 2020

7 VERAM (2013) Research and Innovation Roadmap 2050: A Sustainable and Competitive Future for European Raw Materials.

8 SIRA, Strategic Innovation & Research Agenda. Bio-based Industries for Development & Growth in Europe.

9 Li, H. (1973) The origin and use of Cannabis in eastern Asia linguistic-cultural implications J. Econ. Bot., 28, pp. 293-301

10 J.D. House, J. Neufeld, G. Leson (2010) Evaluating the quality of protein from hemp seed (Cannabis sativa L.) products through the use of the protein digestibility-corrected amino acid score method J. Agric. Food Chem., 58 (2010), pp. 11801-11807

11 Ascrizzi, R et. al. (2019) Valorisation of hemp inflorescence after seed harvest: Cultivation site and harvest time influence agronomic characteristics and essential oil yield and composition. Industrial Crops and Products Vol. 139, 111541

potential of the hemp through intense proteolysis which led to both the release of bioactive peptides and the increase in the protein digestibility.[12]

Due to the sensitive nature of cannabis biomass, companies that are engaging the cultivation and process must undergo strict regulatory guidelines especially on keeping records and disposal of residues. Accounting and destruction of cannabis apply only to regulated plant parts of cannabis notably the above-ground parts of plants, from which the resin is not removed. However, hemp seeds and hemp stems in an isolated state is excluded. An exception has also made for plants or seeds of the same genus if the plant, plant part or preparation has a content of tetrahydrocannabinol (THC) of not more than 0.2%. The current waste management approach for cannabis residue includes incineration, composting, and anaerobic fermentation (i.e. biogas production). Hence, open more opportunities for developing upcycling technology for creating high-value products.

The term Cannabis and Hemp sometime create confusion because both belong to the same plant species. However, they are genetically distinct and are distinguished by their application, and chemical composition (i.e. cannabinoid content) as well as by differing cultivation. Moreover, these cultivars may also share the same molecular and structural components in term to its biomass characteristics and properties. Hence, the term cannabis and hemp used in this report can be interchangeable.

Objectives

In this report, we will outline the current common practices in Denmark regarding cannabis waste management. We will explore in-depth literature review the different biorefining technology and upcycling opportunities to sustainably valorized cannabis residues and investigate their potential applications and prospects. We will also examine some regulations that ensure the proper handling of cannabis waste. In addition, we will discuss the various cannabinoids (i.e. CBD and THC) extraction methodology as well as outline the state-of-the-art downstream unit operations for the purification and concentration of medical cannabis oil products.

1. Upcycling technology

Upcycling is the process of transforming by-products, residue materials, useless, or unwanted products into new materials or products perceived to be of greater quality and higher value. Cannabis cultivation and manufacturing generates an enormous amount of residue that can be upcycled for value-added products. In Canada alone, it was estimated that by 2020 there will be over 6,000 metric tonnes of cannabis waste produced per year. Since the cannabis industry is booming globally (cannabis legalized countries), therefore the vast residues generated could have an unsustainable impact on the environment if it is not utilized or manage properly. In recent developments, the cannabis entrepreneurs are exploring ways that cultivators and processors can turn cannabis plant waste and post-extraction residues into economic advantage.

[12] Pontonio, E. et. al. (2020) Impact of Enzymatic and Microbial Bioprocessing on Antioxidant Properties of Hemp (*Cannabis sativa* L.). Antioxidants 2020, 9, 1258; doi:10.3390/antiox9121258

The European Commission (EC) and the EU-Member States have recently promoted the use of non-food (technical or industrial) biomass, to tackle three bottlenecks within the EU:

- Finding an alternative to dwindling fossil energy resources;
- Reducing our CO^2 emissions to reduce the greenhouse effect;
- Upgrading agricultural surpluses and residues (now called technical or industrial biomass) for non-food applications i.e. chemicals, materials and bioenergy.

In this connection, the integration of the chemical sector with the agricultural sector will grow significantly in the coming decades. At a global level, society is changing already towards a biobased economy. In a biobased economy, biomass replaces a portion of the fossil resources, such as oil, coal and natural gas, for the production of biochemicals, biomaterials and bioenergy. Biomass-derived residues and wastes can be extracted by chemical, physical, microbial or enzymatic treatments to valorized for applications in sectors such as food, health and medicine, chemistry, materials and energy.[13]

The current application for Cannabis biomass especially for industrial hemp includes:[14]

- Hempcrete, i.e., concrete manufactured utilizing hemp, for products such as bricks or utilized in the same fashion as concrete;
- Fiberboard/hemp plywood utilized as a plywood substitute;
- Fibre for a multitude of industrial uses—from construction to insulation;
- Hemp seed oil;
- Hemp paper (e.g., rolling papers);
- De-hulled hemp seed/nut for food products;
- Seed for bird food

Possibilities for upcycling of cannabis residues for various application:

- Cellulose: isolation for potential plastic manufacturing for cannabis packaging
- Hemp cardboard for cannabis packaging
- Lipids, fats and wax for salves, creams, and lip balm
- Waste ethanol for potential re-distillation
- Fuel, including ethanol
- Soil amendment
- Pet products for both wellness and as bedding

Developing cannabis biomass residue into a sustainable source of value-added biochemicals and biofuels will require a flexible cascading technology. Numerous research and development efforts have been performed to create and apply different technologies for the upcycling and conversion of industrial biomass. So far there is no clear trend showing which technology will be the most effective future option. Nevertheless, there are three main conversion routes[6] that can be employed for upcycling cannabis biomass:

- Chemical route: The chemical catalysis is another well-known principle, with different processes (i.e. chemical hydrolysis, and solvent extraction) in use or under development;
- Thermo-chemical route: The first step in the process here is the gasification of the biomass feedstock under high temperature into synthesis gas. This gas can then be

[13] Vandamme E., (2011) Industrial Biomass: Source of Chemicals, Materials, and Energy. Belgian Academy Council of Applied Science (BACAS)
[14] Morrow, K. (2019) One Hemp Cultivator's Waste is Another Business's Opportunity. Hemp Grower.

transformed into different types of liquid or gaseous fuel, so-called "synthetic fuels";

- Bio-chemical route: This process is based on enzymatic and microbial hydrolysis ("bio-cracking") of the biomass (lignocellulosic) material through a variety of microbial actions or their enzymes that hydrolyze the cellulosic matrix into sugars. In a subsequent step of the process, these sugars can be chemically transformed or fermented into bio-alcohols (i.e. bio-ethanol, butanol, methanol,...) or into a wide range of useful biochemicals (e.g. bioplastics, biodetergents, and biovitamines).

The most industrially important chemicals involve catalysis, using inorganic catalysts (e.g. acid hydrolysis, and transesterification).[15] In order to be able to valorize major components of lignocellulosic biomass (cellulose, hemicellulose and lignin), acid hydrolysis is employed as a pretreatment step to recover the cellulose and hemicellulosic sugars for subsequent enzymatic conversion. Various acid hydrolysis or chemical transformation techniques have been studied for pretreatment of lignocellulosic biomass; recently also the use of ionic liquids has been documented with a nearly 90% yield of glucose from cellulose and 70-80% yield of sugars from untreated corn stover. The most promising technology is Ammonia fibre explosion (AFEX) pretreatment, which is a combination of a chemical (i.e. ammonia) and thermo-physical digestion (i.e. temperature and pressure) of the biomass in order to increase the fermentable sugar yields.[8]

Biochemical conversion of biomass is another technology that can be utilized for upcycling of cannabis residues. Biochemical conversion entails breaking down of biomass by using enzymatic and/or microbial action, to make the polymeric carbohydrates available as fermentable sugars, which can then be converted into biofuels, bioplastic (i.e. polylactic acid (PLA) and polyhydroxyalkanoates (PHAs)) and bioproducts using microorganisms (e.g. bacteria, yeasts, and fungi) and their enzymes. In optimizing the role of biochemical conversion, researchers are developing technologies needed throughout the process including new enzymes for hydrolysis and new microorganism for fermentation.[8] It is only now being fully realized by the chemical industry that the utilization of microorganisms is an inexhaustible source of a wide range of useful enzymes and chemical compounds. Several fine and bulk chemicals such as solvents, food additives, enzymes, agrochemicals and biopharmaceuticals are now being produced based on microbial biotechnology via industrial fermentation or biocatalysis processes.[16, 17]

As an example of upcycling agri-residues from crops is the ProEnrich project. This project aims to develop novel functional proteins and bioactive ingredients from rapeseed, olive, tomato and citrus fruit side streams for applications in food, cosmetics, pet food and adhesives. Different biorefining technology was employed for this project to valorize these agri-residues including extraction and fractionation, filtration and purification and drying (Figure 1).[18]

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[15] Serrano-Ruiz J., West R. and Dumesig J. (2010). Catalytic conversion of renewable biomass resources to fuels and chemicals. Ann. Rev. Chem. Biomol. Eng., 1, 79-100.

[16] Gavrilescu M. and Chisti Y. (2005). Biotechnology: a sustainable alternative for chemical industry. Biotechnol. Adv., 23, 471-499.

[17] Demain A.L. (2007). The business of biotechnology. Ind Biotechnol., 3, 269-283

[18] The ProEnrich Project. Bio Based Industries Joint Undertaking under the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 792050.

Figure 1. Generic cascading unit operations for upcycling plant biomass utilized in the ProEnrich project.

Cannabis Manufacturing and processing residue contribute to the securing of a sustainable supply of feedstock for the biobased economy in Europe. This will require further research into methods of improving the biorefining process of biomass for optimal conversion efficiency.

2. Cannabis plant biomass: physicochemical characteristics

Medical cannabis (i.e. marijuana) and industrial hemp are from the same species of plant, *Cannabis sativa*, but from different varieties or cultivars. However, industrial hemp and medical cannabis are genetically distinct and are distinguished by their application, and chemical composition (i.e. bioactive compounds) as well as by differing cultivation practices in their production. Though medical cannabis generally refers to the cultivated plant used as a psychotropic and non-psychotropic drug (i.e. THC and CBD, whether used for medicinal or recreational purposes), industrial hemp is cultivated for use in the production of a wide range of products, including foods and beverages, personal care products, nutritional supplements, fabrics and textiles, paper, construction materials, and other manufactured and industrial goods.[19]

Nonetheless, with more than 1,000 strains of cannabis having been bred over several decades, it is crucial to understand the different physicochemical characteristics of cannabis biomass. Since the medical cannabis is also belonging to the same plant species as the industrial hemp, it can be hypothesized that they also share the same molecular and structural components in term to its biomass characteristics and properties. Although the medical cannabis is not known for its fibre producing anatomy, nevertheless its structural components may be similar or closely related to the industrial hemp. Thus, is it vital to understand industrial hemp biomass's molecular and structural components, to comprehend what type of valuable compounds aside from the cannabinoids that medical cannabis contain especially the residues (i.e. stem, leaves and branches).

Industrial hemp constitutes bast fibre and inner xylem core; its fibre bundles are located in the cortex and encircles the inner core (Figure 2). Hemp is the source of two types of

[19] Congresional Research Service (2019). Defining Hemp: A fact sheet. https://crsreports.congress.gov

natural fibres: bast fibres (fibrous form) and woody core fibers, called hurds or shives (i.e. xylem) and consists of about 20–40% of bast fibres and 60–80% of hurds or shives.[20] The hemp fibres are situated in the bast of the hemp plant (Figure 2). The separation of the bast fibre is carried out through defiberization or decortication i.e. breaking the woody core of the stems into short pieces and separation of bast fiber from the hurds using specialized machinery. The byproduct of the hemp stem obtained after the industrial defiberization process is called chenevotte (constituted from the xylem tissue of the stem, i.e. the shives).[21]

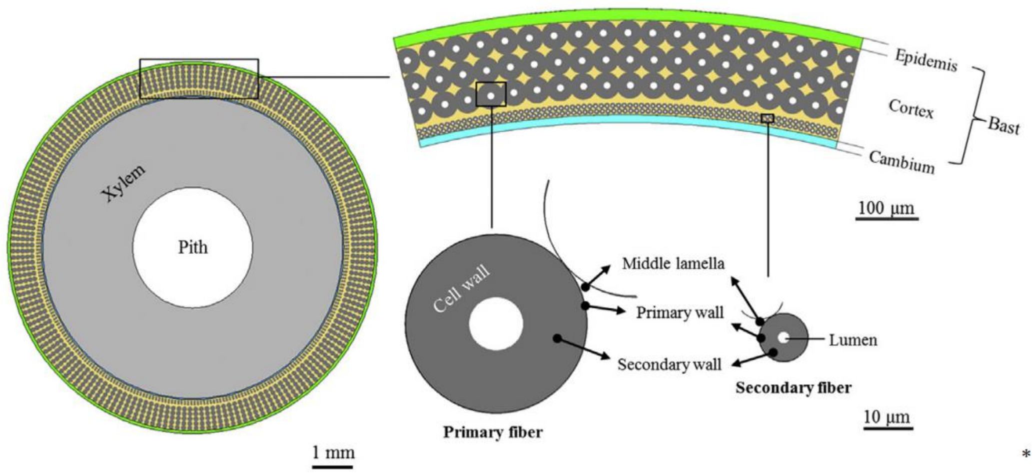


Figure 2. A transverse section of industrial hemp stem showing the structural organization of a bast strip and single fibre (e.g., primary- and secondary fibres) in the bast layer. The xylem tissue of the stem is also known as the shives a byproduct from hemp fibre processing.[7]

The main chemical components of hemp fibre cell walls are cellulose, hemicelluloses, lignin and pectin and the fibres are bound together by pectin and lignin-rich middle lamella.[22] The chemical composition of industrial hemp plant includes over 75% of cellulose, more than 10% of hemicellulose, and less than 10 – 12% lignin. The bast fibres contain higher amounts of cellulose than the hurds ca. 45% (Table 1)[23].

Table 1. Chemical composition of industrial hemp fibres

Hemp Components	Blast Fibres	Hurds or Shives
Cellulose	57 – 77 %	40 – 48 %
Hemicellulose	9 -14 %	18 – 24 %
Lignin	5 – 9 %	21 – 24 %

[20] Stevulova N, et. al. (2014) Properties and characterization of chemically modified hemp hurds. Materials 7:8131– 8150.

[21] Nadia Morin-Crini, et al. (2018) Hemp based materials for metal removal. Green Adsorbents for Pollutant Removal, 19, Springer Nature, pp.1-34.

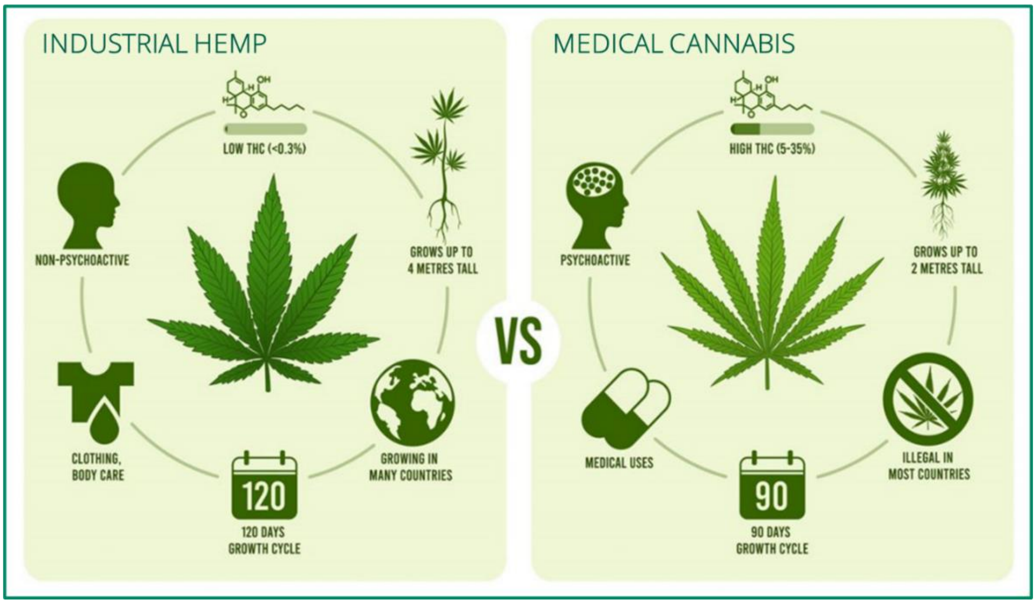
[22] Liu M, Ale MT, et. al. (2015) Effect of harvest time and field retting duration on the chemical composition, morphology and mechanical properties of hemp fibers. Ind Crop Prod 69:29–39

[23] Placet V, Day A, Beaugrand J (2017) The influence of unintended field retting on the physicochemical and mechanical properties of industrial hemp bast fibres. J Mater Sci 52:5759–5777

Industrial hemp seldom requires the use of plant protection and fertilization as it is readily adaptable to all types of soil and temperate climates such as in Europe, hemp is appreciated by organic growers not only for its ease of production but also for its rapid growth i.e. 120–150 days cropping cycle. Fibre hemp may yield up to 25 t above-ground dry matter per ha (i.e. 20 t stem dry matter per ha) which may contain maximum 12 t/ha of cellulose, depending on the genetics (e.g. varieties), cultivation practices, climate and environmental conditions.[24, 25]

2.1 Cannabis morphological attributes

Medical cannabis (i.e. marijuana) and industrial hemp and are both varieties of cannabis, however, they have been cultured for distinct uses and can be distinguished by their chemical and genetic compositions (Figure 3).[26] The term industrial hemp dates back to the 1960s and generally refers to cannabis varieties that are grown primarily as an agricultural crop, such as seeds and fibre and byproducts such as oil, seed cake, and hurds.[27] Hemp is generally characterized by plants that are low in delta-9 THC, the dominant psychotropic compound in *Cannabis sativa*. Industrial hemp generally has high levels of CBD, the primary non-psychotropic compound in *Cannabis sativa*.[28] Genomic research in Canada supports the notion that over thousands of years of cultivation, cannabis farmers have selectively bred *Cannabis sativa* into two distinct strains—one for fibre and seed, and one for medicine.[29]



[24] Bouloc P (2013) Hemp: industrial production and uses. CABI, Oxfordshire, 312 p

[25] Ingrao C, et. al. (2015) Energy and environmental assessment of industrial hemp for building applications: a review. Renew Sust Energ Rev 51:29–42

[26] SDatwyler and Weiblen (2006) Genetic Variation in Hemp and Marijuana (Cannabis sativa L.) According to Amplified Fragment Length Polymorphisms," Journal of Forensic Sciences, vol. 51, no. 2.

[27] See L. Grlic, (1968) A Combined Spectrophotometric Differentiation of Samples of Cannabis, United Nations Office on Drugs and Crime.

[28] Clarke and Merlin (2013) Cannabis: Evolution and Ethnobotany (University of California Press, 2013), p. 255.

[29] ScienceDaily, "How Hemp Got High: Cannabis Genome Mapped," October 24, 2011, citing vanBakel et al., "The Draft Genome and Transcriptome of Cannabis Sativa."

Figure 3. The crucial distinction between medical cannabis and industrial hemp in terms of THH content, growth cycle, physical characteristics, and regulatory acceptance.[30]

It appears that the distinct differences of industrial hemp and medical cannabis (i.e. marijuana) are distinguished by the psychotropic compound it contains. The physiological differences between hemp and marijuana generally include plant height (i.e. industrial hemp is often encouraged to grow tall, however medical cannabis is cultivated to grow short and tightly clustered). The cultivation techniques also differ where the industrial hemp is often grown as a single main stalk with few leaves and branches, whereas medical cannabis is encouraged to become bushy with many leaves and branches to promote flowers and buds. The planting density for industrial hemp is often densely planted to discourage branching and flowering, however, the medical cannabis plants are well-spaced for the branch to flourish.

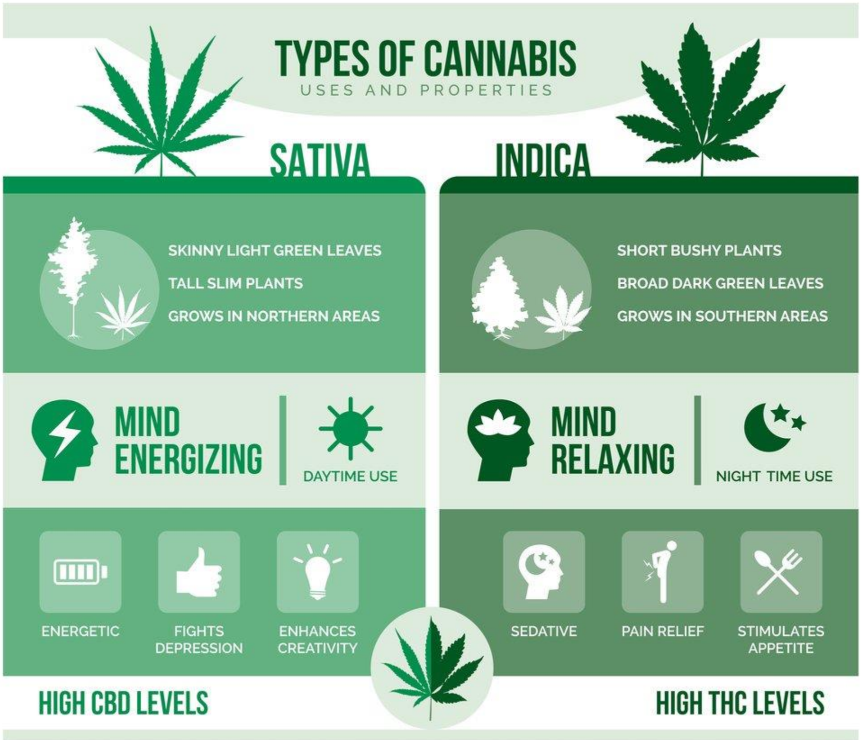


Figure 4. Primary varieties of cannabis notably Sativa and Indica, both of which have unique benefits. Indica and Sativa plants differ in appearance and growth, as well as in their medicinal properties.[31]

Cannabis as a species of flowering herb is split into three subspecies namely Indica, Sativa, and Ruderalis. Ruderalis plants lack potency and are generally small and yield thus being avoided by breeders and cultivators; hence the focus of the medical cannabis community is on Indica and Sativa strains. Indica and Sativa plants differ in their appearance. Indica plants are short and stocky, featuring leaves that are broad and chunky and contain a high THC level. Sativa plants tend to be taller and skinnier and may even be lanky in appearance, with leaves that are thin and pointed and contain high CBD level (Figure 4).

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[30] Hemp vs. Marijuana: A beginners guide.

[31] Rossi, J. (2019) Indica vs. Sativa: Which Cannabis to Use for Which Purpose?

2.2 Commercially interesting cannabis applications

The residues generated from medical cannabis cultivation and manufacturing may include stems and branches. Though the length of the stem of medical cannabis cultivars is shorter compared to industrial hemp, it is noteworthy to point out that medical cannabis plant stem and branches may possess the same structural component i.e. fibres and shives. Hence, the applications proposed for industrial hemp can also be relevant for medical cannabis notably for the residual biomass from cultivation and manufacturing. Industrial hemp fibres have some of the best mechanical properties of all-natural fibres. They are mainly used for speciality pulp & paper, insulation material and for bio-composites in automotive applications. Before the rediscovery of industrial hemp in Europe in the 1990s, industrial hemp fibres were mainly (> 95%) used for speciality pulp & paper.

However, in 2014, hemp pulp & paper supplied mainly by French producers is still the most important market for European hemp fibres with a market share of 55%. Currently, the insulation material is the second most important application for hemp fibres. Insulation material accounts for 26% of the applications or if you take out pulp & paper nearly 60%. Together with other non-woven applications group is 30%, including mulch fleeces which are used in gardens and agriculture, and mats for farrowing pigs. Bio-composites account for 15% of the applications, without pulp & paper 33%. The only established bio-composite market is press (or compression) moulding in automotive interior applications with a share of 96% of all biocomposites. This corresponds to more than 3,700 tonnes of hemp fibre or about 7,500 tonnes of biocomposites (natural fibre content varies between 30 and 70%). Automotive biocomposites for interior applications are still a growing market and are used for door panels/inserts, trunk liners, spare wheel covers, parcel trays, and headliners.[32]

The current most important market for hemp shivs is the high-performance bedding material for horses and other animals like chickens. Hemp shivs can absorb moisture up to 4 times their dry weight. The total Hemp shiv applications equine bedding has a market share of 45% and other bedding 17%. An interesting new and increasing market is using hemp shivs in combination with lime for construction. The market share for shivs is currently 15%. Over the last few years, hundreds of private houses have been built in France, the UK and Ireland with this new material, which can be sprayed into a timber frame construction. The material is easy to handle, price competitive shows good insulation properties for construction material and it appears to be crack-proof, a good attribute for earthquake risk areas. Eco-construction experts especially are seeing great potential in HempLime-Construction. Small amounts also go to the particle-board industry. Hemp shivs can be used to produce lightweight particle boards.[19]

The various applications of hemp plant shown in Figure 5 where each part of this plant can be applied in a specific industrial field. The seeds can be used in the food, feed, and cosmetical field while the stem, it is possible to obtain both shives and fibre, useful for the animal, building, paper and textile applications. The hemp root system is highly developed in comparison to other herbaceous plants, and this feature is suitable for the phytoremediation of soil from heavy metals. Both industrial hemp and medical cannabis cultivars where the flowers and buds are used to obtain products of cosmetic and pharmaceutical interest, such as essential oils containing delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) extracts.[33]

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[32] 2014-05 European Industrial Hemp. Pulp & Paper, Insulation, Biocomposites & Construction, Food & Feed and Pharmaceuticals

[33] Farinon, B. et. al. (2020). The Seed of Industrial Hemp (Cannabis sativa L.): Nutritional Quality and Potential Functionality for Human Health and Nutrition. MDPI Nutrients, 12(7), p.1935. https://doi.org/10.3390/nu12071935

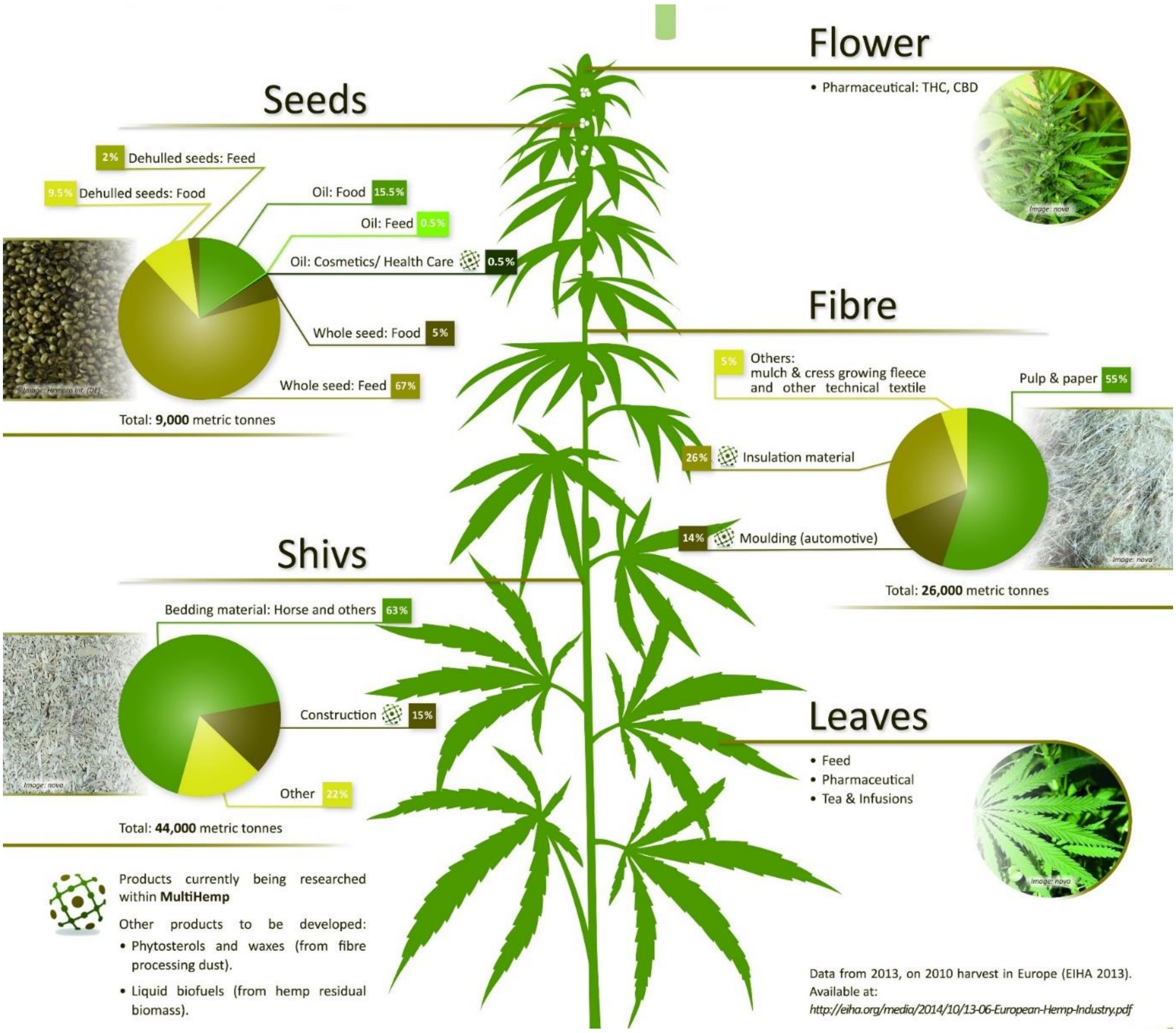

Figure 5. The different parts of Cannabis cultivar outlining the numerous applications and opportunities for various industries notably automotive, construction, and pharmaceutical.

2.2.1 Cannabinoids and its beneficial therapeutic application

Cannabinoids represent the most studied group of compounds, mainly due to their wide range of pharmaceutical effects in humans, including psychotropic activities. Cannabinoids represent a group of C21 or C22 (for the carboxylated forms) and more than 90 different cannabinoids have been reported in the literature, although some of these are breakdown products and they are generally classified into 10 subclasses. The predominant compounds are THCA, CBDA and cannabinolic acid (CBNA), followed by cannabigerolic acid (CBGA), cannabichromenic acid (CBCA) and cannabinodiolic acid (CBNDA). THCA is the major cannabinoid in the drug-type cannabis, while CBDA predominates in fibre-type industrial hemp. Cannabinoids accumulate in the secretory cavity of the glandular trichomes, which largely occur in female flowers and most aerial parts of the plants. They have also been detected in low quantity in other parts of the plants including the seeds, roots, and the pollen, in an extent depending on the drug- or fibre-type of cannabis (Figure 6).[34] Higher THC concentrations are found on the outside surface of the seed coat, possibly as the result of contamination with plant leaves or flowers. Cannabinoids in the leaves have been shown to decrease with the age and along the stem axis, with the highest levels observed in the leaves of the uppermost nodes.

The biological properties related to cannabinoids rely on their interactions with the endocannabinoid system in humans. The endocannabinoid system includes two G protein-coupled cannabinoid receptors, CB1 and CB2, as well as two endogenous ligands, anandamide and 2-arachidonylglycerol. Endocannabinoids are thought to modulate or play a regulatory role in a variety of physiological processing including appetite, pain-sensation, mood, memory, inflammation, insulin, sensitivity and fat and energy metabolism. The psychoactive decarboxylated form of THCA, THC, is a partial agonist of both CB1 and CB2 receptors but has a higher affinity for the CB1 receptor, which appears to mediate its psychoactive properties. The CB1 receptors are also found in the immune cells and the gastrointestinal, reproductive, adrenal, heart, lung and bladder tissues, where cannabinoids can therefore also exert their activities. CB2 receptors are thought to have immunomodulatory effects and to regulate cytokine activity.[35]

	Hairy roots	Root		Seed		Stem		Leaves		Pollen		Flower		*Bedrocan®	*Bediol®
Molecules		Fiber-type	Drug-type	Fiber-type	Drug-type	Fiber-type	Drug-type	Fiber-type	Drug-type	Fiber-type	Drug-type	Fiber-type	Drug-type	Drug-type	Drug-type
THC	1.04[a]			0–12 (<0.5 in kernel)[c] 3–29[d]	36–174 (<2 in kernel)[c] 15–70[d]	196–475[j]	3000[e]	2000[f]	60300[g] 22000[f] 8000[e]		31230[h]	76300[i]	95100[g] 34000–200000[i] 152000[e]	190000[i]	19000[i]
CBD	1.67[a]	14.3[b]		67–244[d]	4.2–78[d]	179[b] 7850–18090[j]		1790[b] 20000[f]	11200[g] 3000[f]		440[h]	8590[b] 6000[i]	10900[g] <600[i]	<600[i]	79800[i]
CBN				2–7[d]	3.4–8.4[d]	0–47[j]			800[g]		1350[h]		600[g]		
CBG	1.63[a]							2000[f]	1000[f]		1310[h]	<600[i]	1000–10000[i]	11200[i]	1700[i]
THCV											510[h]	<600[i]	(<600) – 1300[i]	1300[i]	<600[i]
CBC											3240[h]	4 600[i]	900–2200[i]	2300[i]	5400[i]

Figure 6. The concentrations in cannabinoids found in different parts of the hemp plants, in vitro hairy roots, and some commercial medicinal products.[21]

The cannabidiol (CBD) acts as an important entourage compound as it can reduce the side effects of THC (Englund et al., 2012), and may thereby increase the safety of cannabis-based extracts. It has been shown in in-vitro and animal studies that CBD possesses anti-anxiety, anti-nausea, anti-arthritic, anti-psychotic, anti-inflammatory, and immunomodulatory properties.[36, 37] Cannabidiol (CBD) is a very promising cannabinoid as it has also shown potential as therapeutic agents in preclinical models of central nervous

[34] Andre, Christelle M et al. "Cannabis sativa: The Plant of the Thousand and One Molecules." Frontiers in plant science vol. 7 19. 4 Feb. 2016, doi:10.3389/fpls.2016.00019.

[35] De Petrocellis L., Ligresti A., Moriello A. S., Allarà M., Bisogno T., Petrosino S. (2011). Effects of cannabinoids and cannabinoid-enriched Cannabis extracts on TRP channels and endocannabinoid metabolic enzymes. Br. J. Pharmacol. 163 1479–1494.

[36] Englund A. M., Stone J., Morrison P. D. (2012). *Cannabis* in the arm: what can we learn from intravenous cannabinoid studies? *Curr. Pharmaceut. Des.* 18 4906–4914.

[37] Burstein S. (2015). Cannabidiol (CBD) and its analogs: a review of their effects on inflammation. Bioorgan. Med. Chem. 23 1377–1385.

system diseases such as epilepsy, neurodegenerative diseases, schizophrenia, multiple sclerosis, affective disorders and the central modulation of feeding behaviour.[38] Interestingly, CBD presents also strong anti-fungal and anti-bacterial properties, and more interestingly powerful activity against methicillin-resistant Staphylococcus aureus (MRSA).[39]

2.2.1 Terpenes

Terpenes are responsible for the scent and flavor of the various cannabis strains. Terpenes are classified in different families according to the number of repeating units of 5-carbon building blocks (isoprene units), such as monoterpenes with 10 carbons, sesquiterpenes with 15 carbons, and triterpenes derived from a 30-carbon skeleton. The yield and distribution of terpenes in the plant vary according to numerous parameters, such as processes for obtaining essential oil, environmental conditions, or maturity of the plant. Terpenes form the largest group of phytochemicals, with more than 100 molecules identified in the Cannabis plant.[40]

Terpenes showed a wide-array of pharmacological properties, notably D-limonene which exhibits potent anti-cancer, anxiolytic and immunostimulating properties in humans. The β-myrcene, a terpene also found in the hop, is recognized as a potent anti-inflammatory, analgesic, and anxiolytic component while α-Pinene is an acetylcholinesteral inhibitor, which could counteract the memory deficits induced by THC. The Linalool, commonly found in *Lavandula angustifolia*, possesses similar properties to the ones described for its monoterpene counterparts, i.e., analgesic, anti-anxiety, anti-inflammatory, and anticonvulsant. β-caryophyllene, a well-known active principle of black pepper and Copaiba balsam, possesses potent anti-inflammatory and gastric cytoprotector activities.[21]

3. Biorefinery of medical cannabis biomass

Biorefinery is the sustainable conversion and processing of biomass into a spectrum of bio-based products e.g. food, feed, chemicals, materials and bioenergy such as biofuels, power and/or heat.[41] Biorefinery takes advantage of the various components in biomass and their intermediates (i.e. carbohydrates, proteins, triglycerides) that can be further converted into value-added products, therefore maximizing the value derived from the biomass feedstock.[42] Biorefining of medical cannabis biomass also requires the understanding of the existing industrial applications of another cannabis variety namely the industrial hemp (Figure 7).

Multiple value-added products can be derived from biorefining cannabis biomass residue from cultivation and manufacturing i.e. stem reach fibres and shivs. Cannabis (i.e. industrial hemp) fibres and stalks are used in textiles, and pulp for paper industries, construction

[38] Hill A. J., Williams C. M., Whalley B. J., Stephens G. J. (2012). Phytocannabinoids as novel therapeutic agents in {CNS} disorders. *Pharmacol. Therapeut.* 133 79–97.

[39] Appendino G., Gibbons S., Giana A., Pagani A., Grassi G., Stavri M. (2008). Antibacterial cannabinoids from *Cannabis sativa*: a structure-activity study. *J. Nat. Prod.* 71 1427–1430.

[40] Brenneisen R. (2007). “Chemistry and analysis of phytocannabinoids and other cannabis constituents,” in Marijuana and the Cannabinoids Forensic Science and Medicine ed. ElSohly M. (New York, NY: Humana Press;) 17–49.

[41] International Energy Agency - Bioenergy Task 42. "Bio-based Chemicals: Value Added Products from Biorefineries | Bioenergy".

[42] Biorefinery (2010). In: Biorefineries. Green Energy and Technology. Springer, London. https://doi.org/10.1007/978-1-84882-721-9_3

applications, biocomposites, mulch and animal bedding. Hemp oil derived from the seed, flowers, and buds have a therapeutic application, hence the medical cannabis cultivars are suited for this purpose (Figure 7).

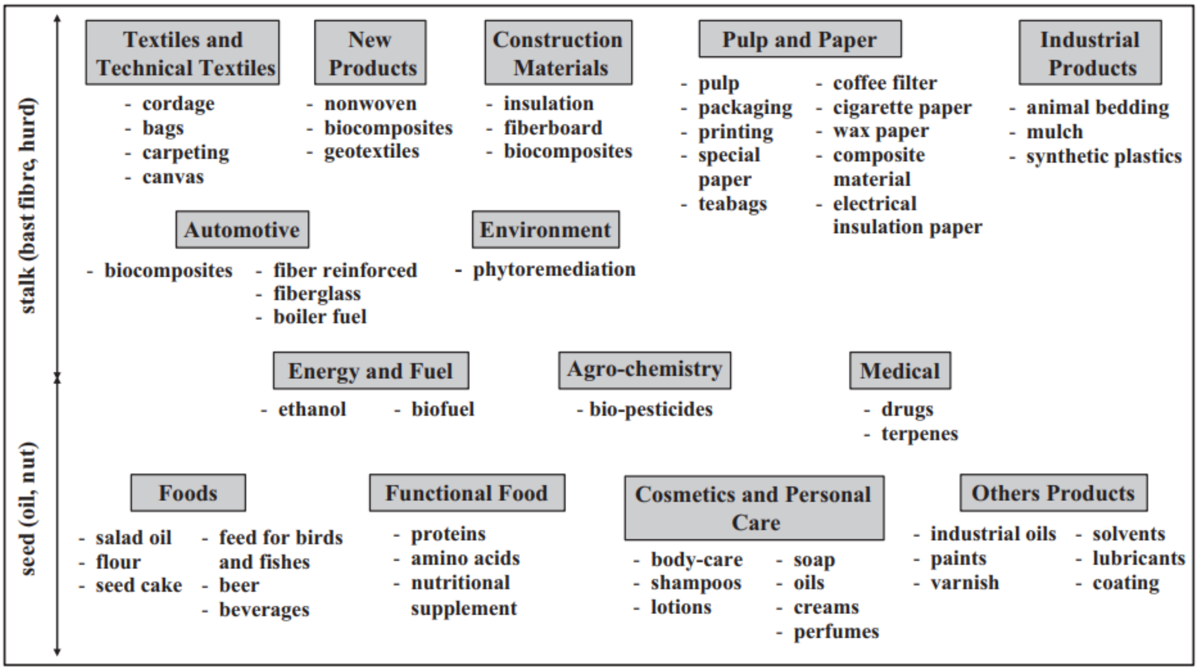

Figure 7. Multiple cannabis i.e. industrial hemp applications and possible products will be developed with biorefining technology for the cannabis plant and residue streams.[8]

While the interest of cannabis has been increasing in recent years, it is mostly centered on the research and development of cultivation and processing of cannabinoids for therapeutic and recreational application. Therefore, it is noteworthy to outline the opportunity and possibility of the utilization of the medical cannabis cultivation and processing residue for upcycling in a biorefinery concept. However, challenges exist because there is only limited if there is any information concerning the biorefining of medical cannabis beside for the medical and recreational application. On the other hand, the Cannabis sativa (hemp variety) for industrial fibre application has already been subject to many biorefinery studies (Figure 7) including integrated production of cellulosic bioethanol and succinic acid.[43]

The most recognized biorefining processing technology for manufacturing of medical cannabis-based products.[44]

- Primary Extraction: The process of removing the desirable plant components (cannabinoids, terpenes) via an organic solvent.
- Degumming: a process that removes phospholipids from a primary extract using a catalyst such as citric acid.

[43] Kuglarz, Mariusz et. al. (2016) Integrated production of cellulosic bioethanol and succinic acid from industrial hemp in a biorefinery concept. In: Bioresource Technology 200. pp. 639-647.

[44] Precision Extract Solution. Ultimate Guide to Producing Hemp and Cannabis Extract.

- Centrifugal Terpene Removal: The process of separating terpenes from a primary extract using a centrifuge device.
- Winterization: The process of removing plant lipids from a primary hydrocarbon extract via a secondary solvent, freezing, and filtration.
- Absorbent/Decolonization/Carbon Scrubbing: The process of removing the dark color and undesirable components of a primary extract via various filtration media.
- Dewax: The process of reducing and removing plant lipids via low-temperature single solvent isolation and filtration.
- Vacuum Purge: The process of removing residual solvents via a low pressured low heat oven cycling.
- Decarboxylation: The process of removing the carbolic acid group from primary cannabinoids via heat.
- De-solventization: The process of removing the solvent from solute of an extract.
- Multi-Plate Chromatography: The separation of a cannabinoid mixture by passing it in solution or suspension or as a vapor (as in gas chromatography) through a medium in which the components move at different rates.
- Co-Solvent Separation: The process of isolating one or more cannabinoids via matching various solvents to cannabinoid polarity.
- Co-solvent Crystallization: The process of isolating cannabinoids via crystallization by matching various solvents to cannabinoid polarity.

This section will discuss the various production techniques and where the most residue accumulation from cannabis production, cannabinoids (i.e. CBD and THC) extraction methodology as well as outline the state-of-the-art downstream unit operations for the purification and concentration of medical cannabis oil products.

3.1 Residues from Cannabis production

The whole cannabis industry is consisting of different business models notably cultivation, manufacturing, distribution, retail, and laboratory testing. Each of these business models can function as a single entity or combinations in the cannabis value chain for producing the final consumable cannabis products. In the cultivation business model, to obtained cannabis flower or buds (i.e. the THC- and CBD-containing part of the cannabis plant), cultivation and growing process must take place until the buds are ready for harvesting. The manufacturing business model comes into play once the flowers or buds are harvested, where the valuable chemical components (i.e. cannabinoids) is isolated using various extraction technologies to produce cannabinoid i.e. THC- or CBD-containing oils. There are several downstream technologies to employ for concentrating, purifying, and converting cannabinoid-containing-oil from its acidic molecular form to an active molecule (i.e. CBDA to CBD).

Concentrated and purified cannabinoid-containing oils (i.e. CBD or THC) can be infused into a variety of consumable cannabis products which can be distributed in many existing industries. In the medical and pharmaceutical sector, THC or CBD infused oils can be marketed and sold as tinctures (e.g. drops). In the recreational sector (not yet legally permitted in Denmark), isolates and purified cannabis-oil can be formulated and infused on a variety of consumable goods including, but not limited to sodas, vape juice, hard candies, gummies, baked and chocolate cakes, while balms and lotions are being promoted in the cosmeceutical sector.[45]

Both the cultivation and manufacturing business generates an enormous amount of waste residues. In the cultivation, the residues are generated from routine pruning, trimming, harvest, cloning, propagation, i.e. flower, leaves, stalk or stem, root ball, failed plant, mature clone until harvesting and curing. The minor residue will be accumulated during packaging and handling of buds and cannabis oil products. Manufacturing of THC and CBD containing cannabis oil also accumulates waste notably from the post-extraction of cannabis biomass that includes buds, flowers, leaves, trims, and shake with allowable levels of residual contaminants or with solvent residuals. In Canada, it was estimated that by 2020 there will be over 6,000 metric tonnes of cannabis waste produced per year. Solid waste from cannabis production, using any production method, can include:[46]

- Green plant material (cannabis flowers, trim, leaves, stalks, and roots);
- Growing media (cocoa, peat, rock wool);
- Growing supplies (plastics associated with potting, propagation, and other typical crop production supplies and their associated packaging); and
- Chemical containers associated with pesticides and/or cleaning agents.

Growing media is typically used for only one growing cycle and can therefore generate a significant amount of waste. Rockwool is not compostable, therefore if the growing media contains rock wool, the rootballs will be surrounded by it and will not be able to be composted. For this reason, some growers avoid using rockwool.

In pursuant to section 9, subsection 9, § 10 and § 63, subsection 2 of Act no. 1668 of 26 December 2017 on the pilot scheme with medical cannabis in Denmark stipulates that raw materials (i.e. buds) that are not used in the manufacture of cannabis intermediates must be destroyed unless the Danish Medical Agency (i.e. Lægemiddelstyrelsen) permits something else.[47] The current cannabis regulation in Denmark does not stipulate on what type of technology a company must carried-out for destroying unused cannabis materials. Nonetheless, it requires a special area intended for the destruction of unused cannabis materials. One issue of concern regarding cannabis waste is whether THC may enter the environment upon solid waste disposal. The range of THC content of various cannabis plant parts (dry weight) are:[48]

- 10-24% in flowers
- 1-2% in leaves
- 0.1-0.3% in stalks
- < 0.03% in the roots.

The cannabis company has the liberty of choosing cannabis waste management strategy that is compliant to the regulatory guidelines. Whether the unused cannabis raw materials also include cultivation and processing residue, this current regulation allows exploring new

[45] How much of a cannabis plant is waste?

[46] Senate of Canada – Senate Standing Committee on Agriculture and Forestry. 42nd Parliament, 1st Sessions, December 3, 2015 to Present. Evidence Briefing: March 27, 2018. Topic: Composting of cannabis residues and potential impacts on the environment.

[47] Bekendtgørelse om import af cannabisudgangsprodukter og fremstilling af cannabismellemprodukter

[48] United Nations Office on Drugs and Crime. 2009. Recommended methods for the identification and analysis of cannabis and cannabis products. Manual for use by national drug analysis laboratories. United Nations Publication Sales No. E.09.XI.15. ISBN 978-92-1-148242-3.

technology and ways on how to manage cannabis residues before the destruction of the biomass (Figure 8).

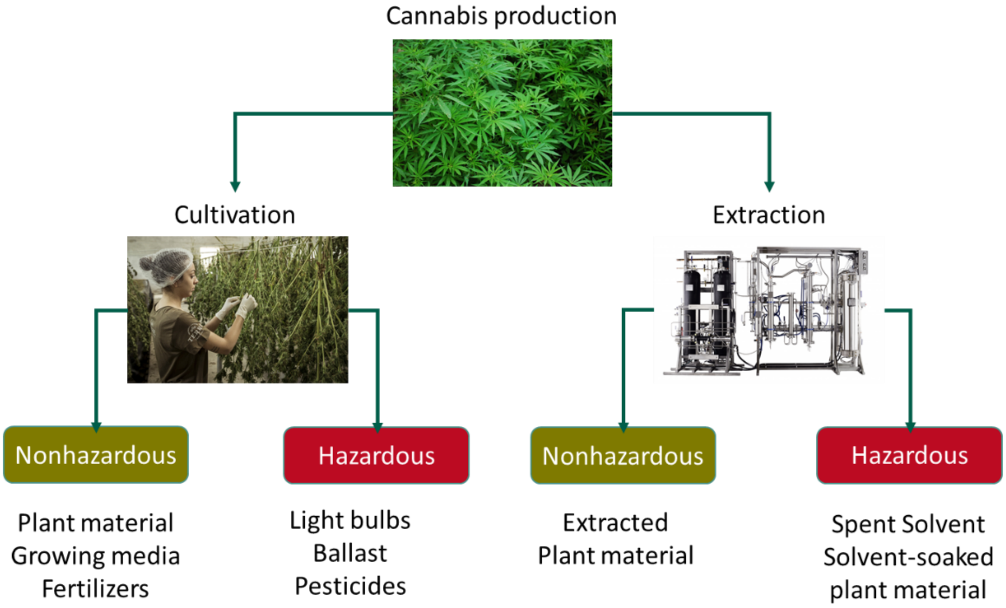

Figure 8. Multiple wastes are generated by cannabis production and processing

Tons of potential contaminants found in cannabis residue streams instituted during cultivation and processing activities such as pest control, fertilization, volatile extraction, and downstream purifications. Cannabis companies are expected to conduct standard waste management operation protocols and methods of analytical waste stream testing to properly characterize their waste. None or only limited studies only been done into the environmental impact of cannabis residues and their chemical constituents. For instance, no published research on the effect of cannabinoids (i.e. THC or CBD) if it leaches into our sewage system or runoff into a water basin, lakes, and beaches. Therefore, cannabis residues streams must be handled in a manner that is sustainable, compliant, and environmentally friendly. Establishing a well-defined waste management scheme and implementing new technology that adds value for cannabis residue streams, businesses can concentrate on product development and marketing strategy while remaining in full compliance. Every part of the cannabis plant whether it comes from cultivation or processing, they eventually turn into waste. Thus, the most challenging aspect for cannabis businesses is to make sure that proper waste management is enforced.

Cannabis cultivators indicated that there is a large amount of growing media waste (i.e. cocoa, peat, and perlite) generated over the cannabis crop cycle. Certain cultivation sites will also use a plug transplant made from rockwool, which is not fully biodegradable. But most of the spent growing media is compostable. A range of production styles exists, and producers may use anywhere from 5 L to 40 L of growing media per plant per cycle. For these calculation estimates, an average of 15 L per plant is used. The following calculation is provided as an example to indicate realistic numbers associated with cannabis growing media production:[49]

- Facility size: 10,000 m^2 (1 hectare)
- Number of plants: 15,000 total or about 1.5 plants per m^2
- Number of crop rotations: 3 per year (4-month growing cycle)
- Growing media: 15 L per plant x 15,000 plants x 3 plant cycles per year = 675,000 L = 675 m^3

Common growing media mixes have a dry bulk density of 750 kg/m^3, but it becomes saturated at the end of a growth cycle, which may have a bulk density of up to 1,000 kg/m^3. Therefore, an annual mass of growing media waste may range from 506 to 675 tons.

On the other hand, plant residues (stems, trimmings) weigh an average of 0.2 kg and yield an average of 1.75 L of green waste per plant or 114 kg/m^3 bulk density. At 1-hectare site with 15,000 plants, as described above: 1.75 L per plant x 15,000 plants x 3 plant cycles per year = 78,750 L per year or 79 m^3 per year. Therefore 79 m^3 of plants would be the equivalent of 5,586 kg per year or 5.5 tons of green waste

3.1.1 Pruning and cuttings

Defoliation or pruning is a gardening technique that is routinely performed during cannabis cultivation (i.e. vegetative growth stage) which allows growers to selectively remove unwanted tissue to direct the growth of the plant into developing huge, beautiful cannabis buds. It removes plant tissue that is damaged and unproductive as well as increases airflow and light exposure minimizes the potential for microbial growth and diseases (Figure 9). Thus, a very essential activity that all cannabis growers must carried-out whether it is an indoor or outdoor cultivated cannabis plant. Technically, it is the cutting off small parts of the cannabis plants in specific time to redirect its energy on nourishing and strengthening the remaining leaves, shoots, and developing quality flowers and buds. Nevertheless, unnecessary pruning can be damaging to the overall wellbeing and development of the cannabis plant. Pruning at the wrong time of the growing cycle or excessive and erroneous pruning of the essential stems and shoots can weaken the plant through stress and inflict damage and subsequently reduce the yield.

[49] Ahearn, T. and P. Larouche. 2018. Composting in the Cannabis Industry. Brome Compost.

Figure 9. Pruning encourages the plant's healthy growth by enabling the plant to focus its energy on developing quality buds. It also promotes greater airflow and light exposure, fostering a more vibrant plant, and forming denser, more cannabinoid-rich buds. Photo: Gina Coleman/Weedmaps

The accumulation of plant residues (i.e. leaves and shoots) from pruning and cuttings takes place during the vegetative phase where the cannabis plant is approximately 30 cm tall (auto-flower). Pruning and cutting parts of the cannabis plant can be carried out in multiple sessions before the flowering stage, thus plant cuttings or residues are also being accumulated throughout the cannabis vegetative stage. To our knowledge, no study or public report that provide an estimated quantity on how much residue is being collected during defoliation, pruning, and cutting. Nevertheless, many cultivators adopted a rule of thumb requiring that never remove any more than one-third of the vegetative parts of the plant in any single pruning session to avoid putting the plant into shock or under stress. Pruning residues might consist of large fan leaves that are pointed toward the interior of the canopy and leaves that are covering multiple flowering sites. This is necessary to avoid shading, so part of the plant that is going to grow are the ones that receive direct light. Severe pruning or taking out more than a third of the vegetative parts of the cannabis plant is detrimental to the wellbeing of the plant especially after it has completely passed its vegetative stage because it will not re-generate those vegetative parts again.

It is challenging to establish how much and what plant residues were accumulated for the entire pruning session unless proper recording of the quantity (kg wet basis), separation and identification of the part of the plant being pruned is carried out and maintained meticulously. Another factor that hinders our understanding of the extent of the plant residue being collected in pruning sessions is probably due to many cannabis cultivation strategies implemented by different growers. A cultivator might choose to grow cannabis from a mother plant or directly from seed. These cultivation strategies require different pruning and cutting regimes, for instance growing with auto-flower seed needs successive pruning until maturity and before flowering. On the other hand, cuttings from the mother plant can be used as seeding and maybe only a few of these cuttings will turn into waste. Nonetheless, it is crucial to determine the quantity and identity of the cuttings being accumulated to established proper documentation which is a prerequisite in the setting-up legal medical cannabis business in Denmark. This will also allow the development of technology necessary to effectively valorized the cannabis cutting residues and determine its valuable components for upcycling.

3.1.2 Harvesting, buds' isolations, and trimming

The flowering stage would take at least eight weeks for indoor cannabis plants, but it takes longer for outdoor cultivated cannabis plants to be ready for harvest. Harvesting of cannabis buds from the whole plant and post-harvest activities notably trimming, drying, and curing is accounted for the highest accumulation of residual plant biomass. About 80% of the original cannabis plant material is removed by the time all the harvest and post-harvest activities are done.[50] During harvest activity, trained harvesters will start cutting and removing the unwanted section of the plant (a.k.a. green waste), and that includes the whole stem, leaves, and branches, and ultimately, all that is left are the flower buds. Thus, the need to properly account for residual plant biomass is crucial to remain compliant with the regulations so they can monitor what is being classified as waste.

Harvesting and post-harvest techniques vary among cultivators, however certain similar steps that every cannabis cultivator should adhere during the harvest process. These steps include removal of the large fan leaves, trimming or removing the remaining leaves near the flowers, and removing the flowers themselves from the stems. Aside from these three steps, which address the physical removal of portions of the plant, other crucial stages of the harvest process include the drying, sorting, and curing of the cannabis flowers. Depending on how large the cultivation area and quantity of plants, harvesting cannabis plants can be a very labor-intensive and time-consuming process. Thus, has many cannabis producers employ computerized and automation devices, which can improve harvest efficiency and lessen some of the labor associated with the harvest.

After the end of the flowering stage, cultivators or growers must check thoroughly and decide that the cannabis plants are ready for harvest. The first residue accumulation in the harvest process is when starting to remove the large fan leaves. The large fan, or sun, leaves are easily identifiable as the stereotypical cannabis leaf. These leaves can be plucked by hand, cut with scissors, or removed with a device, such as a hand-held hedge trimmer (Figure 10). The large fan leaves do not contain a high quantity of cannabinoids (i.e. THC or CBD) unlike the leaves closer to the flowers or the flowers and buds themselves. Many growers simply dispose of these residues for destruction with upcycling to valorize for high-value products. Once the fan leaves are removed, a cannabis grower has two choices: to trim the remaining leaf material while the plant is wet (wet trimming) or to begin the drying process and remove the remaining leaf material by hand or with an automated trim machine after the plant has dried.[51]

Sorting cannabis flowers is also a crucial step in maximizing the efficiency of the harvest process, however, plant residues, as well as rejected cannabis flowers in the sorting process, are accumulated. But the rejected flower due to size and appearance can be utilized as input material in the manufacturing of cannabis oil. Separating the dried cannabis flowers into different sizes allows the cultivator to further process the flowers more effectively and efficiently. Processing the same size flower material in an automatic trimming machine can have a dramatic impact over the entire harvest process, especially for large scale operations resulting in more effective sorting and trimming. Once the

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[50] Whole Plant Harvest

[51] Guide to Cannabis Harvest Processing

cannabis flowers are sorted, they can be further processed in a trim machine or other processing device depending on size. Sorting can also be done after the trimming process is complete. Sorting the trimmed flowers by size can make them more marketable.[9]

Figure 10. Harvest and post-harvest activities where most of the cannabis plant residue (red circles) are accumulated. Around 80% of the original cannabis plant material is removed by the time all the harvest and post-harvest activities are completed. Photo: Spliffseed

Trimming cannabis serves several purposes but also accumulates waste residue namely trims. Cannabis looks better, tighter, more uniform appearance because the removal of excess foliage often results in a final product that is far more visually pleasing. Moreover, fan leaves contain a lesser concentration of trichomes. Removing these protruding leaves reveal parts of the section that have much richer in trichome concentration. Larger leaves jutting from the buds is thicker, moisture-rich and tend to provide a harsher vapor. During the curing process, trimmed buds tend to leave a more uniform moisture content, proving a much more even and flavorful vaporizing experience (Figure 11).

Figure 11. Red circles illustrate the residues that are accumulated during the trimming process. These residues might still contain minor amounts of cannabinoids, hence many processors utilized them for various applications notably hash, kief, rosin, cannabutter or even herbs for pizzas.

3.2 Extraction technology for cannabinoids

The medical cannabis pilot programme in Denmark is intended to provide a better basis to assess the use of medicinal cannabis at the end of the trial period. The programme will allow doctors to prescribe a new type of cannabis product which, until now, was not legal in Denmark. Exactly which products will be available in the pilot programme will depend on the manufacturers of cannabis products. It is the manufacturers who will decide which cannabis products they want to produce and market in Denmark and hence which products doctors can prescribe. So, the cannabis products available may change during the four-year pilot programme. The end products desired to be produced vary substantially depending on the technology, equipment used, solvent and process employed in the production and manufacturing of cannabis-based products.

Current biorefining of cannabis for manufacturing cannabis oil-based employed carrier-oil extraction, such as solvent-based extraction, super- or sub-critical carbon dioxide extraction and light hydrocarbon extraction methods. With cannabinoids being found within the resin glands (trichomes) of female flowers of plants, the manufacturing process is costed up to cannabis oil extraction as well as corresponding downstream operations e.g. separation and purification rather than harvesting i.e. infrastructure set up costs; and operating costs.

Extraction of cannabis-oil or concentrates using hydrocarbon (HC) such Butane, Propane and Pentane solvent is best for certain products notably Shatter, Butter, Live Resin, Sauce, THC-a crystalline and THC HTFSE (high terpene full spectrum extract). On the other hand, cannabis extraction with Ethanol (ETH) as the solvent can produce other products such as

THC Distillate, Full Spectrum CBD (THC free), CBD Isolate, CBD Distillate, and CBD Full Spectrum Extract (low THC).

Supercritical fluid extraction (using CO2) has promising potential for medical cannabis products as this technology can be scalable and adaptable for GMP guidelines. The cannabis-oil concentrates produced by SCF-CO2 have gained more acceptance in the recreational cannabis sector because of its customizability factor. Whether the products are vaporizer pens, salves, infused edibles, or elixirs, most of them were produced using SCF-CO2 extraction technology.[52] Modifying pressure, temperature and solvent ratios, various products can be created ranging from vaporizer-friendly oils to dabbing concentrates such as waxes, crumbles, and even shatters and saps. But the lengthy purification process is required to remove co-extracted constituents, such as waxes and plant fats.

In the previous section, we discussed the importance of understanding the cultivation and harvesting techniques for cannabis. The extend of green-waste residues accumulated during the cultivation and harvesting stage is enormous. On the other hand, manufacturing cannabis-based products also generate a large amount of residue (waste) not only processing waste i.e. solvent and chemicals but also biomass residual waste i.e. trims and buds. Between 2014 and 2017, Washington state (USA) produced 771 metric tons of waste associated with the production and sale of cannabis, including organic waste (i.e. leaves, stalks and roots), extraction materials and solvents, and highly resistant "disposable" packaging. In Canada, cannabis growers have already destroyed 400 metric tons of organic waste, even before 2018's legislation.[53]

Therefore, it is crucial to understand the different processing types and how they are implemented to be able to know the treatment that these residues have been through. In this way, we could be aware of how to process this cannabis processing residue. In this section, we will discuss the manufacturing of cannabis-oil for therapeutic and medical application as this product have enormous application in many industries. We discussed the pros and cons of the common extraction technology employed in the market today notably ethanol extraction, hydrocarbon extraction and sub-supercritical CO2 extraction technology for producing crude cannabis extract. The extraction technology for producing these oils are founded, hence much available literature and experience can be consulted.

3.2.1 Extraction with hydrocarbon solvents

Light hydrocarbons namely butane and propane are the most common hydrocarbons solvent currently used in the biorefining cannabis for extraction of cannabinoids product notably butane hash oil (BHO). The advantages of using light hydrocarbons in cannabinoids extraction are its non-polar characteristics. Butane or propane capture the desired cannabinoids and terpenes without co-extracting contaminants including chlorophyll and plant metabolites. The low boiling point of butane allows to easily purge any residual butane at the end of the extraction process, resulting in a relatively pure product.[54] This method is preferred due to the lower cost of extraction equipment, speed of extraction and ease of production.

[52] Cannabis Extracts and How Are They Made?

[53] The cannabis industry and the difficulty of managing its solid waste

[54] Utilizing Blended Solvents: Butane & Propane Extraction

Current methods of BHO extraction use closed-loop extraction systems that capture any residual butane in the air and recycle it, leaving no butane behind. For some time, an open-loop BHO extraction system was popular because it is quick and low cost. This method places the raw cannabis material and butane inside a metal or glass tube for the separation cannabinoids from the plant material. The butane used in the extraction is released into the atmosphere. Because butane is extremely flammable, a flame or spark can easily cause a deadly explosion. However, in the closed-loop system (Figure 12), the butane used in the extraction is capture and recycles the spent butane for later use. The entire process is much safer, controlled, and effective compared to open-loop extraction.[55] Whatever system used for BHO extraction; they have something in common – the accumulation of residue from the raw material being extracted.

Nevertheless, butane is highly combustible, which have been responsible for the multiple stories of explosions resulting in serious injuries and giving awful image to cannabis extraction industry. In addition, the utilization of low-quality butane can retain an array of toxins in the product or in the extraction residue that can be harmful to humans and the environment when the waste is disposed to landfill.

Figure 12. An example of a closed-loop hydrocarbon extractor. This extractor features individual control of solvent, vacuum, nitrogen, and venting via centralized instrumentation panel for ease of operation. This equipment is C1D1 Compliant & Designed for GMP integration with PSI Certified for 50 State Compliant. This XMU Hydrocarbon extractor model can process up to 100 kg per day shift.[56]

3.2.2 Alcohols extraction

The Food and Drug Administration (FDA) classifies ethanol as a Class 3 solvent with low risk for acute or chronic toxicity in pharmaceutical manufacturing processes where the residual is less than 5,000 ppm or 0.5 %. The FDA also implies that residual solvents in this category

[55] A Guide to Butane Hash Oil Extraction

[56] XMU Hydrocarbon Cannabis Extractor

should be limited to 0.5 % through rigorous quality assurance and quality control programs. The use of alcohols for the extraction of cannabinoids is primarily performed using ethanol or isopropanol. The most frequently used alcohol is ethanol. Ethanol extraction is a single-stream process that may be conducted at hot or cold temperatures. Warm processes tend to extract more plant pigments and waxes, whereas supercooled ethanol processes are more time consuming and less efficient.[57] In addition to the cannabinoid extraction steps, additional dewaxing steps (i.e. winterization) are required for both temperatures.

A typical ethanolic extraction strategy uses either soaking cannabis raw material or pouring/ shower the ethanol in a close vessel. In soaking technique, the dried cannabis material placed inside a filter bag (≥ 200μm) is immersed in the extraction tank filled with cold ethanol at (1:20 ratio depending on the dryness of the material) for less than 20 minutes. On the other hand, the difference with pouring technique is that the cold ethanol (1:10 ratio depending on the dryness of the material) is sprinkled to the dried cannabis material placed inside a 200μm filter bag (Figure 13). The ethanol flows through the biomass and takes the extractable compound along. The flow rate of the sprinkler and the density of the material (i.e. particle size) determines the residence time of ethanol in the extraction tank. In both techniques, the pressure is applied at the end of the extraction to filter all the solution containing cannabinoid out from the extraction tank. With these techniques, the concentrated ethanolic extract is recovered by evaporation using rotary distillation during the downstream process. These systems are expensive to operate for small-scale growers.

Figure 13. Loading of the cannabis plant material into a Pilot-scale extraction vessel. The ethanol is supplied in the vessel either through shower or flooding inside the vessel.[58]

During ethanolic extraction, other chemical components are also extracted along with the cannabinoids. The cannabinoids content of buds, flowers and trims would range from 3.4 to 24%.[59] The typically reported cannabinoid yield is 12 – 20 % depending on the plant

[57] June-Wells, M. (July 2018). Your Guide to Ethanol Extraction in Cannabis. Cannabis Business Times.

[58] The Versatility of the Eden Labs Ethanol Extractor

[59] Andre, C.M. (2016) Cannabis sativa: The Plant of the Thousand and One Molecules. Front Plant Sci. 2016; 7: 19

characteristic, extraction efficiency, downstream process effectiveness and the proportion of cannabis flower, trim, and buds mixed. Thus a 1-ton per day extraction capacity (i.e. at 20 % cannabinoid yield per dry material input) would generate approximately 200 tonnes of dried extracted plant waste annually (i.e. 250 days operations). One challenge with using an alcoholic solvent is that some of the residual alcohol still present in the plant material which needs to be evaporated in a well-ventilated room. This process would also entail more investment for the cannabis processors.

Figure 14. Precision KPD Series: Vulcan - Industrial Cannabis Extraction Plant. This is a close-loop extraction facility where the feed material (i.e. dried cannabis) is soaked in the ethanol, then subjected to a cold press to separate the extract and the solid residue. The ethanolic extract is then filtered and evaporated/ distilled to recover a concentrated cannabis-ethanol extract.[21]

A fully automated industrial-scale technology for cannabis biorefinery using alcohol extraction systems are already available in market notably the Precision KPD Series: Vulcan - Industrial Cannabis Extraction Plant (Figure 14). This multi-unit operation system is a plug and play, meaning that it can be installed in any given location or can be integrated into an existing cannabis cultivation and processing facility. The system can be outfitted with degassing, distillation, and crystallization equipment, depending on lab requirements and fully flexible and customize a cascading system, to meet the desired end-product. The advanced automation and continuous flow capabilities mean it only needs a few technicians to operate the entire production process allowing companies to operate the business with extremely low overhead. The issue with ATEX regulation was resolve with this system since the motor control center and the plant control is separated from the biorefining equipment. Thus, all the electrical components are isolated (i.e. another room) away from the mechanical components that could come to contact with any solvent that is flammable keeping the risk level down.[60]

3.2.3 Supercritical fluid extraction

Supercritical fluid extraction (SFE) is the most effective and efficient technology to isolate valuable constituent from botanical biomass. It is a commonly used biorefining technique in large scale extraction of essential oils and other compounds. The supercritical fluids are highly compressed gases, which have combined properties of gases and liquids in their critical phase. The most commonly used supercritical solvent is carbon dioxide (CO_2). Supercritical fluid extraction is the process of separating one component (the extractant) from another (the matrix) using supercritical fluids for instance CO_2 as the extracting solvent. CO_2 is inexpensive, generally recognized as safe, and has well-known physicochemical properties.[61] Supercritical CO_2 is also nontoxic, nonflammable, and has excellent operational safety.[62] The extraction conditions for supercritical CO_2 are above the critical temperature of 31°C and critical pressure of 74 bars. Owing to its density, diffusivity, and viscosity properties supercritical CO_2 can disperse a large amount of the desired compound(s), penetrate in tiny spaces of the plant matrix, and has very low flow resistance.

The supercritical CO_2 can be used to target more specific compounds than hydrocarbons or ethanol by manipulating its density and polarity. This is possible since the extractive properties of supercritical CO_2 are regulated by temperature and pressure conditions. An advantage of supercritical CO_2 is that each compound has a unique solubility profile related to the density of supercritical CO_2. Thus, if the critical density is known for the target compound, the compound can be individually extracted, removed, and/or separated. The solubility profiles can also be used to separate multiple components of supercritical CO_2 extraction.[63] By altering the temperature and pressure conditions of the extraction site, certain compounds will “fall out” of the solution as the density of the supercritical CO_2 is decreased.[64]

Biorefining of cannabis using SFE with CO_2 is advantageous as it can design a selective process because of CO_2 density being easily manipulated i.e. temperature, pressure, and composition. In processing viewpoint, CO_2 is easy to handle and recover at ambient temperature which doesn’t need another unit operation for solvent recovery and rarely reacting with a component that is being extracted. However, the extraction process takes a longer time as opposed to other solvents (i.e. ethanol) and it requires several downstream processing steps notably extract winterization and filtration to removed residual lipid and waxes from the plant material (Figure 15).

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[60] Precision Extraction Solution. Industrial Cannabis Extraction Equipment. The Evolution of Cannabis Extraction.

[61] Rovetto & Aieta (2017) Supercritical carbon dioxide extraction of cannabinoids from Cannabis sativa L. The Journal of Supercritical Fluids. 129, 16-27

[62] Raber, J. C., Elzinga, S., & Kaplan, C. (2015). Understanding dabs: contamination concerns of cannabis concentrates and cannabinoid transfer during the act of dabbing. The Journal of Toxicological Sciences, 40(6), 797-803.

[63] Salerno and Valsamis (2020) An Environmental Analysis of Recreational Cannabis Cultivation & Processing. Worcester Polytechnic Institute (WPI), Academic Report.

[64] June-Wells, M. (2018). Your Guide to Supercritical Extraction. Cannabis Business Times.

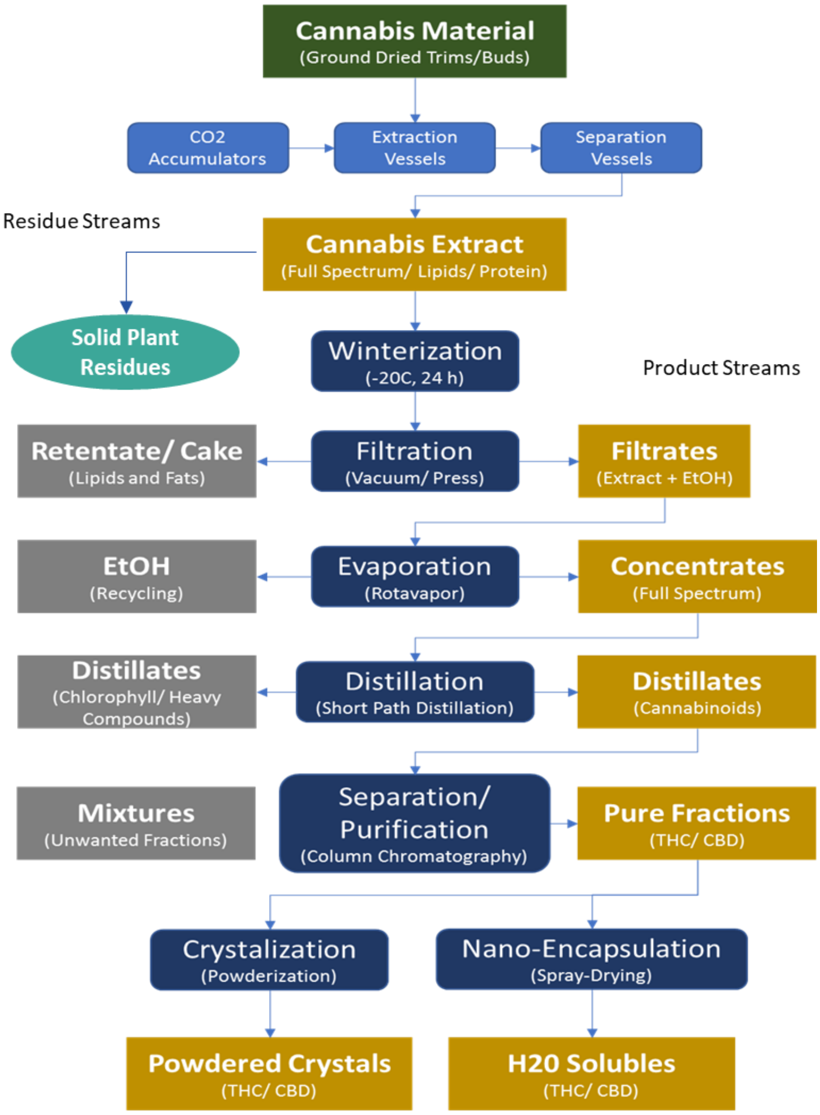

Figure 15. Schematic diagram of Supercritical fluid extraction with CO_2 and downstream processing steps for producing purified cannabis-based products.

A study that explored some process conditions for the extraction and isolation of cannabinoids including THC, CBD, cannabinol (CBN) and cannabigerol (CBG) suggest that the SFE with CO_2 process is the preferred extraction over traditional solvent (hexane) extraction from an economic and ecological point of view.[65] In an industrial scale operation of the supercritical CO_2 process, the CO_2 is recycled, with most units captured up to 95% of the initial CO_2. Hence, the only solvent waste involved in this method is the CO_2 that leaks from the system or are contained in the extract (Attard et al., 2015). The most beneficial aspect of this technique is that it produces a "solvent-free extract,".[66] CO_2 reaches a supercritical state at 31.1℃ and 7.39 MPa and will return to a gas state under ambient conditions. This allows for any residual CO_2 to be removed fairly simply, resulting in a

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[65] H. Perrotin-Brunel (2011). Sustainable Production of Cannabinoids with Supercritical Carbon Dioxide Technologies,.Technische Universiteit, Delft,

[66] Aladić, K., et. al. (2015). Supercritical CO2 extraction of hemp (Cannabis sativa L.) seed oil. Industrial Crops & Products, 76, 472–478.

solvent-free product.[23] The highest yield was reported for the pilot-scale set-up at 40°C and 23 bar with a 6 kg/h (100 g/min) CO_2 flow using samples of 45 g, with a minimum solvent to feed ratio (S/F) of 400:1.[27]

3.3 Downstream processing of cannabis extracts

As discussed earlier, several biorefining technologies for cannabis extraction can generate a wide range of cannabis extraction products e.g. concentrates. The plant genetic make-up and type strain provide a major role in the manufacturing of cannabis compounds (cannabinoids, terpenes, flavonoids) at varying formulations. As in the case of supercritical fluid extraction with CO2, the process can be designed to separate the desired compounds of interest for certain applications. Using such technology, the end-product can be targeted to have a distinctive profile notably aromatic, taste, texture, and bioactive properties.

As depicted in the schematic extraction process in Figure 15, cannabis extracts can also contain contaminant components such as lipids, waxes, and chlorophyll, which is co-extracted from the plant material. Though these components might be useful for some applications, there is often a need for further purification of the extract to remove these contaminants. This can be true whether the purpose is to preserve the profile of compounds (e.g. entourage effect) or to purify distinct compounds from the concentrates.

3.3.1 Winterization and filtration of cannabis extract

Similar to other terrestrial plants, cannabis also contained compounds such as plant waxes, fats, lipids, and chlorophyll which can be liberated during the extraction process. These components i.e. wax, lipids, and fats can alter the chemical makeup of the distillate and, over time, cause it to become cloudy. Removing these components will enhance the purity of the targeted cannabinoids, making them more transparent and increasing the purity of THC/CBD in the final product. Winterization is a downstream process employed for cannabis oil purification process to remove fats, waxes, and lipids from extracts. Hence the process of winterization of oil will purify crude cannabis extracts, thus, increasing the quality and flavor of the resultant oil.

Most primary extraction methods employed such as butane, propane, and CO_2 are nonpolar solvent that will dissolve hydrophobic non-polar components of plant material. Cannabis winterization process involves mixing cannabis extract (obtained from non-polar solvent extraction) with ethanol (a polar solvent) and freezing the solution at sub-zero temperatures allowing the undesirable compounds e.g. waxes to coagulate and solidify. The mixture is then passed through a filter for separating the coagulated wax, lipids, and fats from the oil. The final step involves removing the ethanol from the solution. The finished product of winterization, also known as de-waxing, is considered a winterized extract.[67]

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[67] Cannabis Dictionary: Winterization.

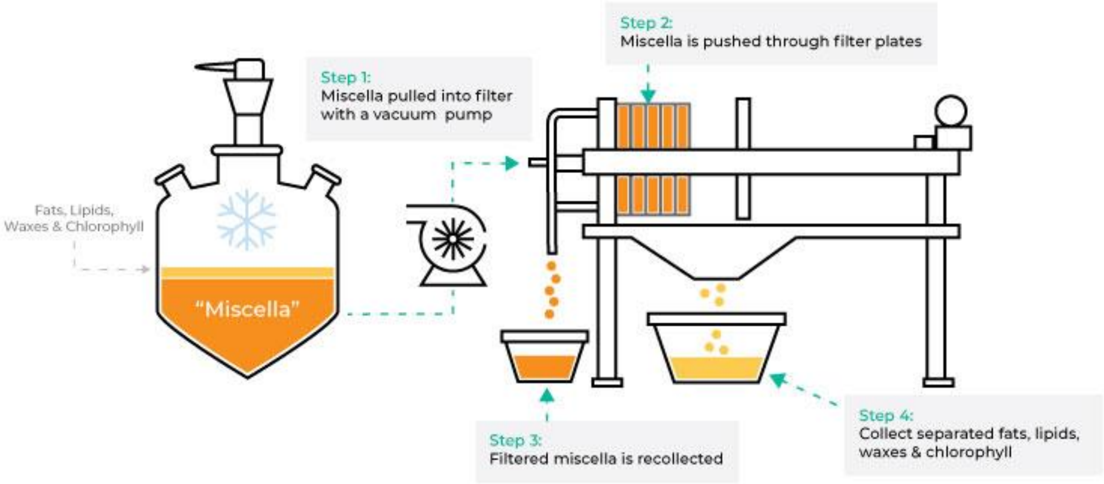

Figure 16. Cannabis Filter Press device for post-winterization filtration of miscella or crude cannabis oil, as well as fines filtration. The press has the option to add up to 5 more filtration plates, easily doubling the throughput. This is great for scalability, making it a reliable fit for labs of all sizes and production capacities in need of cannabis filtration.

The volume of ethanol that is utilized in the winterization process is less compared to the quantity of ethanol used during an ethanol extraction. For instance, 450 kg of cannabis raw material requires 3000 L ethanol. In contrast, 450 kg of cannabis raw material containing 10% cannabinoids will produce approximately 45 kg of CBD oil which requires 450 L of ethanol for winterization.[68] When the lipids have precipitated to the surface of the solution (i.e. floating wax), filtration can be initiated. Filtering is normally assisted by a vacuum to help pull the miscella through the filter (Figure 16). The filtration needs to occur quickly as well since it must stay cool to assure the lipids and waxes don't dissolve back into the solution. Not maintaining the correct sub-zero temperatures will cause the waxes, lipids, and fats to not separate, and the winterization process cannot efficiently be completed.[69]

3.3.2 Solvent recovery and distillation technology for cannabis oil

After winterization and filtration, the solution at this stage is crude oil suspended in 5-10 volume of ethanol. The solvent recovery process is to separate the ethanol from the crude cannabis oil and recover the ethanol for reuse. The process involves heating the mixer in a container at a relatively low temperature so that only the ethanol evaporates and condenses. The classic example of this is a rotary evaporator, where large round bottom flasks are held in warm baths under vacuum to evaporate and condense ethanol. The size of the flask has restricted the efficiency of this process. Therefore, for industrial-scale, other types of evaporators such as falling film evaporator or thin/wiped film evaporator play a crucial role. The ethanol recovery rate can reach to a few hundreds or thousands of liters per hour by these methods.[70]

There are only a few options for the distillation process when manufacturing pure CBD isolates or a product that preserves cannabinoids properties and characteristics. But there

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[68] Extrakt Lab. What You Should Know About Filtration, Winterizing Wax and CBD Extraction?

[69] Precision Extraction Solution. What is the Winterization Process in Cannabis Extraction?

[70] Hydrion Scientific (2019) Post-extraction and pre-distillation processes.

are two different technology available for cannabis concentrates distillation notably the short path and wiped film technology which varies in cost, technology, and scalability. Both technologis use vapor pressure (vacuum depth) to reach the lowest possible boiling points to avoid degrading the compounds of interest.

The Short path distillation utilizes an apparatus with a multi-position receiver and condensing head. This process is very limited in scale and production but can produce high-quality distillate with an experienced operator. Crude oil is heated in a boiling flask with a magnetic stirrer. The condensing head is jacketed and requires a recirculating chiller to cool the condensing head to condense the cannabinoid vapor back into a liquid form.[71] The compounds are then separated through slow thermal heating with precise and controlled temperatures. As the boiling flask temperature slowly raises, multiple fractions of the distillation can be generated—the higher temperature applied, the different compounds will be distilled, starting with highly volatile terpenes or solvent leftover at lower temperatures. Raising the temperature will create a new compound/fraction, and the multi-position receiving flask can be adjusted to collect the different fractions into different receiving flasks. A short path will typically have 3 fractions—heads (terpenes and high volatiles), main body (THC/CBD), and tails (high boiling point cannabinoids).[33]

On the other hand, wiped film distillation is a modified of short path distillation technology, which can operate in batches or continuous modes thus, suitable for high throughput production. While under vacuum, the crude oil is added to the top of a heated vertical cylinder on a rotating plate. Specially designed wipers wipe the oil, thus creating and renewing the thin film. This thin film enables an efficient heat transfer, even for highly viscous fluids. As the oil enters the cylinder, it encounters the rotating, specially designed wipers or rollers that create and renew a thin film on the heated surface. A long, condenser in the middle of the wipers in the evaporator body, cooled with recirculating fluid, condenses the vapor. Receiving vessels collect the distillate and the high-temperature residue at the bottom. A recirculating heater provides temperature control of the feed container and outer jacketed wiped film evaporator body. Refrigerated circulators cool the condenser and cold trap. Optimizing the feed rate, vacuum, and temperatures are essential to yield the desired component composition in the distillate. This method reduces the exposure time of the oil and can increase productivity if it is run in a continuous mode.[33]

4 Cannabis residues management and regulations

Commercial cannabis operations must adhere to strict disposal guidelines. The commercial production and manufacturing of cannabis for the medical application is an emerging sector of Denmark. This section outlines the best practices and available technologies that can sustainably help to minimize the environmental impacts associated with the cultivation and processing of medical cannabis. Moreover, this will also give us insight into what challenges and opportunities that lie ahead to the cannabis industry in Denmark. It is crucial to our understanding that the cannabis industry is exceptionally active thus we can only show a snapshot of the current regulatory guidelines concerning the waste and residue management for cannabis.

[71] Precision Extraction Solution. Cannabis Distillation: Short Path vs Wiped Film.

4.1 Current waste management practice for cannabis producers

Solid waste from cannabis production can be categorized as either green (plant material) or non-green (rockwool, plastics). Some countries classify cannabis plant waste as hazardous if THC concentrations are greater than 10% dry weight, but in Denmark is >0.2%. These high concentrations are typically found in the valuable flower, and inflorescence and are therefore not included in most plant wastes post-harvest. If an entire crop were to be disposed of due to disease or other contamination, then the THC levels may be high in the green waste material and therefore should be treated according to regulatory guidelines.

The principles of the Best Available Control Technologies (BACT) is one of the pollution control methods covered by the U.S. Clean Air Act which is applied for the cannabis industry in the USA and Canada. Best available also means best practicable, meaning there is a cost-benefit analysis of the use of technology. There are three crucial waste management tools for cannabis solid residues disposal are examined by Upland Agricultural Consulting for the cannabis industry in Canada notably British Columbia:[72]

- Composting either on-site or through transportation to a composting facility off-site.
- Incineration, which creates gases and hot air, which can be used for heating the cultivation facility.
- Fermentation or biogas, which produces gas and a digestate. The liquid fraction may be used as a fertilizer; however, the solid fraction will still require disposal.

COMPOSTING: Most waste elements of cannabis production can be composted including leaves, trimmings, roots, and coco-coir, but not rockwool. The Compost Council of Canada believes that composting should be the preferred method to process cannabis residuals. Cannabis plant material is high in carbon; therefore, it will require a nitrogen source for successful composting. Pellet and powder forms are a safe option, but externally sourced nitrogen feedstocks can increase the risk of introducing pathogens into the system if the finished compost will be used in the operation.[59]

The costs associated with composting range widely, with simple on-farm setups costing under $5,000 to large scale commercial composting facilities requiring multi-million-dollar investments. Regardless of the scale of operation, composting is not an autonomous activity. It requires management and oversight to monitor moisture levels and carbon: nitrogen ratios, among other factors. Composting can significantly reduce the volume of crop waste and transform it into a soil amendment and/or nutrient resource for other crops. Furthermore, composting can prevent greenhouse gas emissions that would occur if the material were otherwise transported to a landfill. Therefore, when managed properly, composting can be a very environmentally effective BACT.[59]

INCINERATION: The process that involves the combustion of organic substances in an enclosed vessel at high-temperatures and converts the waste into ash, flue gas and heat is called incineration. A technology that can destroy cannabis plant material into ashes. The ash is mostly formed by the inorganic constituents of the waste. Incineration of cannabis may only be carried out after approval by the Danish Medicines Agency and under the Agency's control for permission for destruction (section 13 of the Executive Order on Narcotic Drugs) in Denmark.

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[72] Upland Agricultural Consulting (2019) Commercial Cannabis Production in British Columbia: Best Available Control Technologies and Regulatory Oversight of Environmental Considerations.

Incinerators often have two burn chambers. The primary chamber is where the material is initially combusted, and a secondary burn chamber then combusts unburned gases and particulates (Figure 17). This secondary burn process is intended to reduce stack emissions and comes at a cost for added equipment and burner fuel. The effectiveness of a secondary chamber to reduce stack emissions varies based on what is being burned and how well the incinerator is designed. Some manufacturers claim that cannabis byproducts can be reduced to just 3-5% of their original volume as ash.

Figure 17. The Matthews Environmental Solutions mobile incinerator. The incinerator is fitted, along with a generator and fuel tank on to a flatbed trailer. To speed up start-up preparation time, the incinerator incorporates a hinged chimney to enable it to lie horizontally during transportation.[73]

Product specifications indicate that 540ºC may be adequate to burn with no visible emissions. Burn rates are 10 kg/hr of material for the smaller incinerator models and up to 750 kg/hr for the largest model. A mid-range model would be able to burn 70 kg/hr of plant material using 15 L/hr of diesel. Outside installation is recommended with a simple metal roof or three-sided metal shelter, providing a minimum of four feet of clearance from any combustible roof materials. Incinerators can also be placed in a shipping container, placed on a trailer to be mobile (Figure 17). Incinerating can lead to the development of fine particulates, and the remaining ash requires disposal. There is a high level of fossil fuel consumption associated with incineration, but the by-product of incineration is energy, which can be converted into hot air for heating or hot water for cleaning/washing.

[73] Matthews Environmental Solutions Company. Available online: Trailer Mounted.

FERMENTATION: Cannabis residue can be treated anaerobically onsite using a dry anaerobic digestion (>20% dry matter) process.[74] Each digester is an airtight box, heated to a stable 37ºC. The process, which takes 6-8 weeks, involve microorganisms that break down biomass (e.g. leaves, stems) in an oxygen-free environment. Fermentation occurs in four steps: hydrolysis, fermentation (acidogenesis), acetogenesis, and methanogenesis.[61] The resulting product is biogas, and wet residue called digestate. Several digesters can operate in parallel to allow a constant treatment of waste over time. The system is tolerant to the input of sand, fibres, and large particles.

The positive benefits of fermentation are that a low level of gases created and the liquid fraction of the digestate may be used as nutrient-rich fertilizer and is often referred to as a probiotic. Applying different pretreatment techniques allows us to increase and accelerate the production of biogas. However, there may be high costs associated with the disposal of the remaining solid digestate or sludge. Alternatively, it may be land-applied as a soil amendment if an appropriate-sized land base is available. The commercial-scale digesters require approximately 600 m2 of space and can accommodate 2,000-30,000 tonnes of waste per year. Anaerobic fermentation is an effective method at reducing the volume and weight of solid cannabis waste. Other than the need to dispose of the solid fraction after digestion, there are few, if any, negative environmental impacts associated with dry anaerobic processing: the power requirements are low, there are no engines or pumps required.[59]

A study was carried out on industrial hemp straw residues to assess the effective performance of this feedstock in biogas production by reproducing the real operating conditions of an industrial plant. An organic loading rate was applied according to two different amounts of hemp straw residues (3% wt/wt and 5% wt/wt). The increase of the specific gas production of biogas due to an increment of the organic loading rate (5% wt/wt) was +77.9% without enzymatic treatment and it was +129.8% when enzymes were used. The best management of the biodigester was found in the combination of higher values of hemp straw residues coupled with the enzymatic treatment, reaching 0.248 $Nm3 \cdot kgvolatile\ solids^{-1}$ of specific biogas production. Comparisons were made between the biogas performance obtained within the present study and those found in the literature review showed that hemp straw performance was similar to those provided by previous studies on a laboratory scale.[75]

4.2 Regulations of handling of euphoric substance in Denmark

In pursuant of section 17(2) of the executive order on euphoriant substances, companies in Denmark undertaking activities with cannabis under the medicinal cannabis pilot programme and the development scheme must keep a register of purchase, sale, use and destruction of cannabis. Every quarter, companies that cultivate cannabis must also report the harvested and used quantities of cannabis to the Danish Medicines Agency according to section 18(5) of the executive order on euphoriant substances.[76, 61] Record keeping and destruction of the regulated parts of cannabis is a crucial activity for companies engaging in the cannabis business in Denmark.

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[74] Wageningen University. Anaerobic fermentation. Accessed December 2020

[75] Asquir, C. et. al. (2019) Opportunities for Green Energy through Emerging Crops: Biogas Valorization of Cannabis sativa L. Residues. Climate 7(12), 142.

[76] Danish Medical Agency. Record-keeping and destruction of medicinal cannabis.

The destruction of the regulated parts of cannabis meant a process where a euphoric substance (THC) in a material is decomposed into a non-euphoric substance or where the material with the euphoric substance is destroyed (e.g. incineration) and the residual material no longer contains a euphoric substance with more than 0.2% THC. Destruction of cannabis may only be carried out after approval by the Danish Medicines Agency and under the Agency's control (section 13 of the Executive Order on Narcotic Drugs). This means that for each quantity of cannabis that is to be destroyed must be applied for permission for destruction from the Danish Medicines Agency. In this connection, the Danish Medical Agency will decide whether we will monitor the destruction.[60]

Regulated plant parts grown in the development scheme or experimental scheme may only be used for this purpose specified in the permit. Unregulated plant parts can be used for purposes that are not medical or scientific, such as the sale of seeds, isolated stems (fibres) and roots. Nevertheless, other legislation, such as pharmaceutical, food, cosmetics, or environmental regulations, may prohibit or set additional requirements for the marketing of cannabis-based products.[60]

4.2.1 Recommendation from the Danish Medical Agency on cannabis products and residues

All companies in Denmark carrying out activities with medicinal cannabis that the destruction of regulated cannabis plant components may only take place upon prior approval from the Danish Medicines Agency and under the agency's control (section 13 of the executive order on euphoriant substances). This means that for every quantity of cannabis the company wishes to destruct, the company must seek approval for destruction from the Danish Medicines Agency.

The detailed information on the requirements for destruction, including destruction method, is provided by the Danish Medical Agency (in Danish only).[77] In brief, accounting and destruction of cannabis apply only to regulated plant parts of cannabis according to the Executive Order on Narcotic Drugs List A (BEK nr 950 of 23/06/2020),[78] by which is meant all the above-ground parts of plants belonging to the genus Cannabis, from which the resin is not removed. Excluded, however, are fruits of the hemp plant (hemp seeds) and hemp stems in an isolated state. An exception has also been inserted in section 1 of the same executive order. 3, no. 7 valid from 1. July 2018: Euphoric drugs do not include plants and parts of plants of the genus listed in list A as No. 1 (i.e. Cannabis) and preparations made from plants or seeds of the same genus if the plant, plant part or preparation has a content of tetrahydrocannabinol (THC) of not more than 0.2%.[60, 61]

Non-regulated plant parts should not be included in accounts for narcotics or in applications for destruction. When accounting for or destroying cannabis plants that contain unregulated plant parts, the company must apply a conversion factor so that only regulated plant parts are accounted for. In practice, for example, the company could remove unregulated parts such as roots (underground parts), seeds and hemp stem (fibres) in an isolated state before the remaining part is destroyed. The exception in § 1, para. 3, no. 7 applies from the time the plant is harvested.[60, 61]

Before any destruction of regulated parts of cannabis, the company must consider whether any waste from the production of cannabis (i.e. residues or whole batches due to quality

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[77] Laegemiddelstyrelsen. Destruktion og regnskab for virksomhed med tilladelse til dyrkning af cannabis til medicinsk brug.

[78] BEK nr 950 af 23/06/2020. Bekendtgørelse om euforiserende stoffer.

problems) is regulated. If the waste does not contain more than 0.2% THC, it is not regulated and then the company can send the waste to regular disposal or possibly use it for new products, including selling it to others companies that can process it into other products.

Nevertheless, if the company's waste contains more than 0.2% THC, then the company must consider whether it can remove so much THC so that the content falls below 0.2%, or whether it will instead destroy the material. When the company must have destroyed cannabis material with more than 0.2% THC, then it must obtain a permit from the Danish Medicines Agency's and carried out a documented process that meets the definition of destruction set by the agency. The company can choose to use public incineration at the incinerator, the as most other companies with narcotics products use. It must then follow the current guidance on the destruction of narcotics. But it can also choose to develop its method of destruction at the company. It requires that the company validates the method – i.e. that it documents that the method removes THC from the plants in the chosen way to 0.2% or less. When the company has thus destroyed the plant by removing THC, then it would be able to sell the residual product or consider it waste.[60]

When accounting for cannabis plant material and applying for destruction, the weight must always be stated on a dried basis. This applies regardless of whether it is non-dried cannabis, cannabis extracts, cannabis extract in capsules, cannabis solutions, etc. This is done by applying a conversion factor. The company must determine the conversion factors for its cannabis products, and these must be documented for each type of cannabis that is handled in an accounting and destruction context. Conversion factors of non-dried cannabis may depend on several elements such as water content and water activity.[60]

4.2.2 GACP and GMP regulations for medical cannabis in Denmark

The Danish Medicines Agency has established specific legislation that aims to ensure control of cultivation and manufacture, to obtain a uniform product which is manufactured in a quality-correct manner, every time. When companies cultivate cannabis in Denmark, they must comply with the rules on good agricultural and collection practice (GACP), and when they produce cannabis products, they must comply with good manufacturing practice (GMP). Ensuring the level of quality of the medicinal product, the rules of good distribution practice (GDP) must be maintained throughout the distribution chain. This means that transport and storage must be controlled, and a traceability system must be established to identify any counterfeit products (i.e. blockchain technology such as Vechain or Cardano)). Most companies employ specialists and consultants to ensure continuous compliance with these strict rules. The requirements imposed on companies will depend on the activities the company will be allowed to perform. These requirements are specified to ensure that only cannabis products of sufficiently high quality are dispensed for the treatment of patients.[79]

[79] Danish Medicines Agency. Medical Cannabis Pilot Programme.

5 Value-added compounds from cannabis residues

Both the medical cannabis and industrial hemp cultivation in North America and Europe have multipurpose applications. The stalks or stems generate fibers and hurds (i.e. woven and non-woven), while the flowers, buds and seeds are being processed for medical, food and feed applications (i.e. protein from pressed seed cake). Economic sustainability of cannabis cultivation and processing should encompass the possibility of recovering the non-narcotic secondary metabolites from residues (stem, leaves, buds and branches) originating from pruning and trimming protocols. This strategy will pave the way for the valorization of the unexploited sections of the cannabis plant through upcycling and biorefining technology.

Cannabis is a multipurpose, sustainable, and low environmental impact crop which can be useful for several applications, from the agricultural and phytoremediation to food and feed, cosmetic, building, and pharmaceutical industries. Indeed, from this highly versatile plant, it is possible to obtain various products of industrial interest such as fibre and shives; bio-building and thermal insulating materials; seeds, flour and oil with important nutritional and functional features; and bioactive compounds of pharmacological interest.[80] The commonly known commercial cannabis-based products in countries that legalized cannabis utilization for recreation and medicinal purposes.

- Crude: low-quality primary solvent extract to be refined to make distillate.
- Shatter: cannabis extract with a hardened and glass-like consistency.
- Butter: cannabis extract with a cake batter type consistency containing a moderate amount of terpenes
- Live Resin: cannabis or hemp extract made with fresh frozen material generally in butter-like consistency containing a high amount of terpenes.
- Sauce: extract that contains a mixture of THC-a isolate/crystals mixed with isolated terpenes.
- HTFSE (High Terpene Full Spectrum Extract): extract containing the highest possible amount of original terpenes normally in a syrup-like consistency which may also contain naturally occurring THC-a crystallization forms.
- THC Distillate: A distilled and isolated form of cannabinoids created via fractional distillation.
- Full Spectrum CBD (THC Free): A CBD primary extract containing a full spectrum of cannabinoids and terpenes of which the THC level is undetectable.
- CBD Isolate (THC Free): The molecular isolate form of CBD obtained via crystallization.
- CBD Distillate (THC Free): a purified form of CBD obtained via fractional distillation having an oil-like consistency.
- Full Spectrum CBD (Low THC): CBD primary extract containing a full spectrum of cannabinoids and terpenes of which the THC level has tested below 3%.

Traditionally, cannabis plants were cultivated primarily as a fibre crop for the production of textiles and ropes, especially in the western world. Despite their high nutritional value,

[80] Irakli M, Tsaliki E, (2009) Effect of Genotype and Growing Year on the Nutritional, Phytochemical, and Antioxidant Properties of Industrial Hemp (*Cannabis sativa* L.) Seeds. Antioxidants (Basel). 17; 8(10)

hemp seeds were initially considered as a by-product of the fibre production, and hence, they were mainly used as animal feed.

5.1 Proteins and dietary fibres from cannabis seed and its potential applications

Medical cannabis cultivar produced cannabinoids rich flowers and buds while industrial hemp is a source of nutritious seeds that have been used as human food for thousands of years. Industrial hemp seeds contain nonmedicinal levels (<0.3%) of the psychoactive THC and, therefore, are different from medicinal cannabis. Presently, hemp seed is processed mainly by mechanical pressing to extract the valuable oil (ca. 25–30%) containing a high (>90%) proportion of unsaturated fatty acid and a desirable balance of ω-6/ω-3 fatty acids. The hempseed pressed cake (i.e. residue) is used to produce various protein-rich food products mainly composed salt-soluble globulins or edestin (~75%) and the water-soluble albumin (~25%), having high biological and functional value.[81, 82]

Industrial hempseed proteins have a high level of arginine and a sulfur-rich protein fraction, two unique features that impart high nutritional values (Table 2).[83] Functional property evaluations have shown that hemp proteins form high-quality emulsions with oil droplet sizes similar to those of milk-based emulsions. Hemp seed protein concentrate has been shown to have >70% solubility at pH 4.0–6.0, whereas most plant proteins are typically insoluble. Addition of hemp seed protein to polycystic kidney disease rat diet led to reduced pathological intensity of renal disease and amelioration of associated cardiovascular impairment. Moreover, hemp seed enzymatic hydrolysates have proven effective during in vitro and in vivo tests as antioxidant and antihypertensive agents. Therefore, hemp seed proteins and hydrolysates have the potential to be used as ingredients to formulate functional foods.[84]

Aside from protein, carbohydrates and dietary fibres are key features of hempseed. Dietary fibre is defined as the part of plant material in the diet, which is resistant to enzymatic digestion and that includes cellulose, non-cellulosic polysaccharides such as hemicellulose, pectin, gums, mucilage and a non-carbohydrate component, namely lignin. The total carbohydrate of hempseed can range between 20 -30 %.[85, 86] Most parts of the total carbohydrate of the hempseed was constituted by dietary fibre, the most of which was the insoluble fraction. In particular, Callaway found a Total Dietary Fibre content (TDF) of 27.6 g/100 g of seeds,[63] demonstrating that the entire carbohydrate fraction consisted in dietary fibre, whereas in the study of Mattila and co-workers,[64] the TDF of hempseed amounted to 33.8 ± 1.9 g/100 g of seeds, representing the 98% of the total carbohydrate.

The high content of Insoluble Dietary Fibre (IDF) was found also by Multari and co-workers for hempseed flour, which resulted in an IDF content of 25.49 g/100 g, whereas the Soluble Dietary Fibre (SDF) content was 0.16 g/100 g, thus highlighting that hempseed is one of the

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[81] Leonard, W.; Zhang, P.; Ying, D.; Fang, Z. (2019) Hempseed in food industry: Nutritional value, health benefits, and industrial applications. Compr. Rev. Food Sci. Food Saf. 2019, 19, 282–308.

[82] Wu, G.; Bazer, F.W.; et. al. (2009) Arginine metabolism and nutrition in growth, health, and disease. Amino Acids, 37, 153–168

[83] Girgih, A.T., Udenigwe, C.C. & Aluko, R.E. (2011) In Vitro Antioxidant Properties of Hemp Seed (Cannabis sativa L.) Protein Hydrolysate Fractions. J Am Oil Chem Soc 88, 381–389.

[84] Aluko, R.E. (2017) Chapter 7 - Hemp Seed (Cannabis sativa L.) Proteins: Composition, Structure, Enzymatic Modification, and Functional or Bioactive Properties. Sustainable Protein Sources p 121 – 132.

[85] Callaway J.C. (2004) Hempseed as a nutritional resource: An overview. Euphytica. 140:65–72

[86] Mattila P, Mäkinen S, et. al. (2018) A Plant Foods Hum Nutr.; 73(2):108-115

richest sources of IDF among several high-protein crops such as green pea, buckwheat, and fava bean (IDS, 8.69 ± 0.07 g/100 g, 6.98 ± 0.01 g/100 g, and 9.39 ± 0.30 g/100 g, respectively).[87]

Table 2. Percentage amino acid composition of hemp seed protein isolate (HPI), hemp seed protein hydrolysate (HPH), and membrane ultrafiltration fractions.[61]

AA	HPI	HPH	<1 kDa	1–3 kDa	3–5 kDa	5–10 kDa
ASX	11.81 ± 0.69	11.39 ± 0.03	9.49 ± 0.06	11.70 ± 0.29	12.79 ± 0.47	12.70 ± 0.11
THR	3.54 ± 0.22	3.68 ± 0.29	3.60 ± 0.04	3.77 ± 0.35	4.01 ± 0.19	4.00 ± 0.19
SER	4.78 ± 0.26	4.63 ± 0.09	4.73 ± 0.21	4.79 ± 0.19	4.69 ± 0.07	4.47 ± 0.38
GLX	22.39 ± 2.23	20.06 ± 1.34	15.18 ± 0.96	19.31 ± 1.04	22.71 ± 1.58	22.87 ± 1.02
PRO	4.13 ± 0.54	4.00 ± 0.07	3.19 ± 0.33	4.04 ± 0.56	4.23 ± 0.11	4.89 ± 0.73
GLY	4.38 ± 0.22	4.29 ± 0.23	3.23 ± 0.06	3.93 ± 0.07	4.54 ± 0.20	4.71 ± 0.44
ALA	4.14 ± 0.21	4.47 ± 0.16	4.91 ± 0.06	4.77 ± 0.12	4.30 ± 0.19	4.12 ± 0.09
CYS	1.49 ± 0.04	1.32 ± 0.23	0.29 ± 0.13	0.66 ± 0.01	1.26 ± 0.07	1.58 ± 0.28
VAL	4.14 ± 0.14	4.66 ± 0.02	5.67 ± 0.14	5.26 ± 0.11	4.45 ± 0.19	4.24 ± 0.14
MET	2.36 ± 0.02	1.81 ± 0.39	1.94 ± 0.04	2.03 ± 0.06	1.85 ± 0.14	1.80 ± 0.15
ILE	3.67 ± 0.35	3.84 ± 0.07	4.15 ± 0.13	4.16 ± 0.11	3.98 ± 0.05	3.90 ± 0.04
LEU	5.51 ± 1.23	6.75 ± 0.04	9.91 ± 0.06	7.26 ± 0.10	5.15 ± 0.04	4.82 ± 0.43
TYR	3.09 ± 0.44	3.45 ± 0.00	4.78 ± 0.02	3.50 ± 0.02	3.06 ± 0.06	3.62 ± 0.96
PHE	3.66 ± 1.10	4.60 ± 0.04	7.68 ± 0.05	5.01 ± 0.14	3.21 ± 0.02	2.85 ± 0.40
HIS	2.65 ± 0.23	2.78 ± 0.03	2.61 ± 0.06	2.47 ± 0.01	2.47 ± 0.03	2.49 ± 0.08
LYS	2.96 ± 0.30	2.97 ± 0.06	3.19 ± 0.11	2.94 ± 0.14	2.56 ± 0.03	2.51 ± 0.07
ARG	13.91 ± 0.55	14.07 ± 0.40	13.87 ± 0.11	12.96 ± 0.13	13.60 ± 0.25	13.31 ± 0.24
TRP	1.39 ± 0.02	1.23 ± 0.16	1.58 ± 0.01	1.44 ± 0.15	1.16 ± 0.12	1.11 ± 0.02
HAA	33.60 ± 2.03	36.13 ± 0.79	44.10 ± 0.84	38.14 ± 0.13	32.64 ± 0.98	32.95 ± 1.11
PCAA	19.51 ± 1.08	19.82 ± 0.36	19.67 ± 0.16	18.37 ± 0.00	18.62 ± 0.19	18.31 ± 0.24
NCAA	34.20 ± 2.92	31.45 ± 1.04	24.67 ± 0.90	31.00 ± 0.75	35.50 ± 1.10	35.56 ± 1.12
AAA	8.14 ± 1.56	9.28 ± 0.12	14.05 ± 0.02	9.95 ± 0.31	7.42 ± 0.19	7.58 ± 0.58

5.2 Polysaccharides from cannabis residue and its potential applications

In general, terrestrial plants like cannabis possessed lignocellulosic biomass that consists of cellulose, hemicelluloses, and lignin. Cellulose and hemicellulose are a polymeric form of carbohydrates (i.e. cellulose and xylan) which can be broken down to monosaccharides, such as glucose, mannose, galactose, and xylose. Through the biorefining process, polymeric carbohydrates notably the polysaccharides can be converted into oligosaccharides and monosaccharides. The oligosaccharide can be utilized as a prebiotic agent while the monosaccharides can be fermented for bioenergy and bioplastic (i.e. PLA and PHA) applications.

As presented above, the typical chemical composition of cannabis plant includes over 75% of cellulose, more than 10% of hemicellulose, and less than 10 – 12% lignin. The bast fibres contain higher amounts of cellulose than the hurds ca. 45%.[10] Table 3 show the monosaccharides composition of cannabis blast fibre and shivs (i.e. woody core).

[87] Multari S., Neacsu M. (2016) Nutritional and Phytochemical Content of High-Protein Crops. J. Agric. Food Chem. 64:7800–7811

Table 3. Monomeric composition of the polysaccharides obtained from cannabis biomass.

Cannabis Biomass	Total	Glucose	Xylose	Galactose	Arabinose	Mannose
Blast fibre (%)	68.9	52.0	7.7	3.5	2.7	3.0
Shivs (woody core, %)	71.6	44.5	25.2	1.5	0.4	n.d

Cannabis woody core eg. shivs and hurds present high monosaccharides content than blast fibre (Table 3). This is of enormous importance in fermentations of lignocellulose-derived sugar streams, as many microorganisms show carbon catabolite repression phenomena. However, this residual material (i.e. shivs or hurd) obtained after fiber extraction and has only minor applications (Figure 18). Hemp shivs have high water-absorbing ability and thus is commonly used as such as animal bedding, garden mulch or in light-weight concrete.[19] Nevertheless, increasing biorefinery studies are now focused on its application as feedstock for bioenergy production.[88, 89] The fermentability of shivs C6 and C5 sugars streams has been demonstrated by producing n-butanol and lactic acid as platform molecules for fuel and bioplastic production. Fermentative lactic acid production is well established and its market size is over 4 mtons per year.[90]

The fermentative production of lactic acid by the *Basillus coagulans* strain seemed promising since high conversion yields and product titers were obtained from both C5 and C6 sugars streams. Moreover, the selected strain showed favorable features such as high substrate concentration tolerance, low nutritional requirements, thermostability and high L-lactic acid enantiomeric excess. For instance, a newly isolated *B. coagulans* C106 strain, produced 215.7 g L^{-1} of L-lactic acid from xylose in fed-batch mode, with a 95% lactic acid yield and 99.6% optical purity.[61] With more C5 sugars (i.e. xylose) in the cannabis residue notably shivs and hurds indicating that there is a potential utilization this biomass in the bioplastic industry.

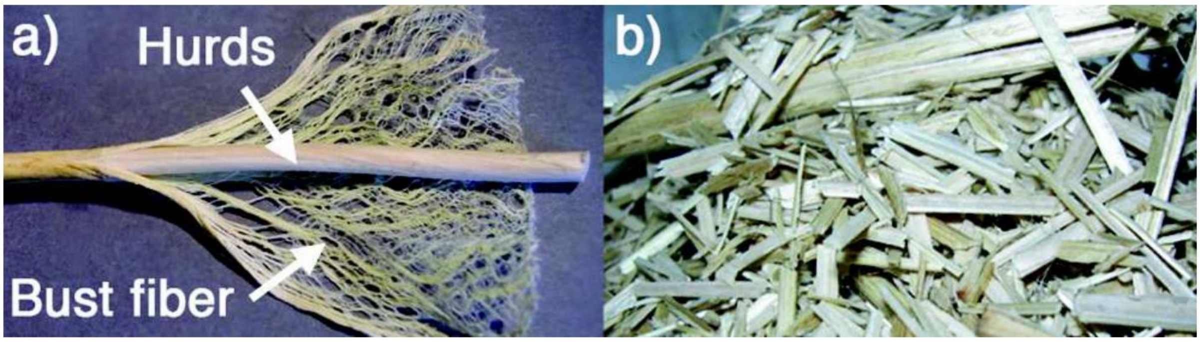

Figure 18. Cannabis stem showing the (a) blast fiber and hurds (woody core), (b) after the woody core (i.e. hurd or shivs) is the separation process of blast fibre.

[88] Rehman, M.S. (2013) Potential of bioenergy production from industrial hemp (Cannabis sativa): Pakistan perspective, Renewable and Sustainable Energy Reviews, Elsevier, vol. 18(C), pages 154-164.
[89] Prade, T. et. al. (2012) Energy balances for biogas and solid biofuel production from industrial hemp. Biomass & Bioenergy. Volume: 40, pp 36-52.
[90] Gandolfi, S. (2015) Hemp hurds biorefining for chemicals production. Dottorato di ricerca in biotecnologie Xxviii ciclo.

The biocomposites and bioplastics are prices competitive in high-quality interior concepts although cannabis fibres are also in competition with flax, jute and kenaf fibres. They are also considered less expensive than fiberglass counterparts and show the favorable mechanical properties of rigidity and strength in combination with low density. Currently, industrial hemp presents a great opportunity for supplying a sustainable and carbon positive source of plasticizing material and several hemp-based plastics or bioplastics are on the market, e.g., in the automotive sector. Cannabis can be processed into different forms used in automotive interior and exterior applications, e.g., carmakers are currently using hemp composite inserts, trunks, headliners, spare wheel covers, parcel trays, etc. An important market is the press moulding market for interior applications: door panels and car boot trims, rear shelf and roof liner panels, dashboards, pillar trims, seat shells, underbodies and other applications.[91]

5.3 Fibers from cannabis residue and its potential applications

Natural fibres from medical cannabis and industrial hemp fibres represent a sustainable solution to be used for different applications in building construction, mainly because of their hygrothermal properties. Biobased materials from cannabis can be manufactured into a variety of commercial products of various densities that resemble concrete, wood, and even plastic. In addition to the environmental value of using plant biomass, these materials benefit from the mechanical strength of the hemp fibres. Cannabis fibres are mainly used for insulation, e.g., insulating material and insulation wool, and/or construction (Figure 19). These fibres can also be used for acoustic and soundproofing purposes. This is an area of research that is currently in full expansion.[62]

High-quality building canna-blocks are produced by mixing a binder, e.g., lime, clay or cement, with non-fibrous shivs or hurds particles.[92] These materials are biocomposites referred to hemp concrete, hempcrete or hemp-lime. Hemp shives in combination with lime is currently another increasing market for construction, e.g., stucco/plaster production, caulking. Hemp provides all sorts of building materials: blocks and bricks, slabs and paneling, wallboard, fiberboard, roofing tiles, and insulation products. Hurds/shives are used to produce light concretes and mortars for different end uses, e.g., wall construction, insulation, underfloor, etc. (Figure 19).

[91] Crini, G., et al. (2020) Applications of hemp in textiles, paper industry, insulation and building materials, horticulture, animal nutrition, food and beverages, nutraceuticals, cosmetics and hygiene, medicine, agrochemistry, energy production and environment: a review. Environ Chem Lett 18, 1451–1476.

[92] Walker R, Pavía S, Mitchell R (2014) Mechanical properties and durability of hemp-lime concretes. Constr Build Mater 30:340–348.

Figure 19. Biobased materials derived from cannabis fibres and shivs notably concrete blocks, panel boards, hemp wood and whole complex build mostly of materials from cannabis.

5.4 Lipids from winterization and purification its potential applications

Cannabis and hemp have a lot of compounds within the plant—such as plant waxes, fats, lipids, and chlorophyll. These compounds are co-extracted and must be removed from the crude oil before the distillation. Not removing these will lower the purity of the targeted cannabinoids you are trying to capture. The process employed in the cannabis industry for this purification stage is winterization. Winterization of cannabis extract is a process that uses a solvent and cold temperatures to separate lipids and other desired oil compounds from waxes. Winterization is a type of fractionation (also known as fractionating crystallization), the general process of separating the triglycerides found in fats and oils, using the difference in their melting points, solubility, and volatility.

Lipids represent the most important component of cannabis inflorescence and hempseeds, particularly from an industrial point of view. Indeed, since hempseeds are oilseeds, the oil is the main medical and food product of industrial interest. Nevertheless, the residue from the winterization process of oil extracted from cannabis buds that may contain some premature seeds also composed of fats, waxes and lipids. Several studies demonstrated that the oil content of hempseeds belonging to different cultivars ranges from 25 to 35% of the whole seed.[93] The seeds belonging to different industrial hemp cultivar highlighted that this variation is mainly due to the genotype. In addition, it was also observed that

[93] Vonapartis E., et. al. (2015) Seed composition of ten industrial hemp cultivars approved for production in Canada. J. Food Compos. Anal. 39:8–12.

even environmental conditions such as geography, climatic conditions, and local agronomic factors affect the total oil content, though slighter than genotype.[94]

The literature data showed that hempseed oil is characterized by high polyunsaturated fatty acids (PUFAs) content and low saturated fatty acids (SFAs) contents. Depending on genotype and environmental factors, hempseed oil contained up to 90% unsaturated fatty acids, of which from 70% to over 80% is composed by PUFAs.[95] The major monounsaturated fatty acid (MUFA) was oleic acid (18:1, n-9) which has been shown to reach the highest value (18.78%) in the Canadian cultivar,[96] whereas the lowest oleic acid content (8.42%) was found in the Finola cultivar grown in Italy.[97] Among PUFAs, Linoleic Acid (18:2, n-6, LA) was the most representative fatty acids in hempseed oil of all analyzed genotypes, accounting for more than half of the total fatty acids. The second prominent PUFAs was α-linolenic acid (18:3, n-3, ALA). Hence, hempseed oil represents an especially rich source of these two fatty acids which are known as Essential Fatty Acids (EFAs), since they cannot be synthesized by mammals and, therefore, must be acquired by diet because they are necessary to maintain healthy human life.[98]

Conclusions

This report provides an overview of the cultivation and manufacturing processes, including valorization opportunities, and explored the issues and challenges associated with cannabis residue management. The focus of the report is on the description and discussion of valuable compounds that can be valorized from cannabis residues while highlighting the best available control technologies for the management for cannabis residues.

The plant-based food market is expected to grow to €2.4 bn by 2025 from €1.5 bn in 2018, and hemp represents the perfect source of sustainable protein to be grown locally and organically.[99] Hemp has been a traditional source of nutritious food in Europe for centuries. All parts of the plant, except the stems, were consumed by humans. While seeds are particularly rich in high-quality proteins and have a unique essential fatty acid spectrum, flowers and leaves are rich in precious phytochemicals (cannabinoids, terpenes and polyphenols), leading to a healthy lifestyle. Recent clinical trials have identified hempseed oil as a functional food, and animal feeding studies demonstrate the long-standing utility of hempseed as an important food source.

The real added value of industrial hemp is its wide array of different application purposes including food, feed, cosmetics, construction materials, biobased plastics, textile and energy. Moreover, cannabis production has the potential to achieve positive environmental impacts. If used as an alternative to carbon-based raw materials, hemp would allow us to capture and store a substantial amount of CO_2. One tonne of harvested hemp stem

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[94] Irakli M, Tsaliki E, (2019) Effect of Genotype and Growing Year on the Nutritional, Phytochemical, and Antioxidant Properties of Industrial Hemp (*Cannabis sativa* L.) Seeds. Antioxidants (Basel). 8(10)

[95] Vonapartis E., et. al. (2015) Seed composition of ten industrial hemp cultivars approved for production in Canada. J. Food Compos. Anal. 39:8–12.

[96] Lan Y., Zha F. (2019) Genotype x Environmental Effects on Yielding Ability and Seed Chemical Composition of Industrial Hemp (*Cannabis sativa* L.) Varieties Grown in North Dakota, USA. J. Am. Oil Chem. Soc. 96:1417–1425.

[97] Galasso I, Russo R, et. al. (2016) Variability in Seed Traits in a Collection of Cannabis sativa L. Genotypes. Front Plant Sci. 7:688.

[98] Farinon B, et. al. (2020). The seed of industrial hemp (*Cannabis sativa* L.): Nutritional Quality and Potential Functionality for Human Health and Nutrition. Nutrients. 12(7):1935.

[99] European Industrial Hemp Association, EIHA. Hemp is the perfect crop for the circular bioeconomy of the future.

represents 1.6 tonnes of CO_2 absorption. On a land use basis, using a yield average of 5.5 to 8 t/ha, this represents 9 to 13 tonnes of CO_2 absorption per hectare harvested.[51]

This report also pointed out that the cannabis plant has various product application of industrial interest such as fibre and shives; bio-building and thermal insulating materials can be derived from biorefining cannabis biomass residue. For instance, industrial hemp seeds contain nonmedicinal levels (<0.3%) of the psychoactive THC and, therefore, have potential for oil, protein, and oligosaccharide production. Hemp oil contains high (>90%) proportion of unsaturated fatty acid and a desirable balance of ω-6/ω-3 fatty acids. The hempseed pressed cake (i.e. residue) is used to produce various protein-rich food products mainly composed salt-soluble globulins or edestin (~75%) and the water-soluble albumin (~25%), having high biological and functional value.

Upcycling opportunities are enormous for the medical cannabis industry based on the various valuable components that can be produced through various biorefining technology that is presented in this report.